Medical Tribune

and Medical News

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Study of Chronic Use of Marijuana Demonstrates No Chromosome Breaks, Brain Damage, or Untoward Effects

Medical Tribune Report

NEW YORK—A double-blind clinical study of the effects of marijuana in a sample of a population long habituated to its use has yielded no evidence of significant physiologic or psychoneurologic differences between smokers and a control group of nonsmokers.

The study, which was commissioned by the U.S. Department of Health, Education, and Welfare to obtain controlled clinical evidence, so far lacking, about the effects of chronic—as opposed to acute—use of cannabis, was carried out on the island of Jamaica by the Research Institute for the Study of Man, New York, in collaboration with the Faculty of Medicine, University of West Indies, Kingston.

The results of this investigation appear to lay at rest many common beliefs about the deleterious effects of marijuana—beliefs based on laboratory observations (or anecdotes) of acute effects in haphazardly collected groups of study subjects, without regard for idiosyncratic physiologic differences or behavioral or sociologic background.

The project was begun in June, 1970, with a broad and intense 18-month anthropologic study to define typical marijuana smokers in representative Jamaican communities, and the final report, *Effects of Chronic Smoking of Cannabis in Jamaica*, embracing physiologic field studies

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L. Cornitas

Analysis of the movements of farmers working cooperatively suggests that muscular coordination is impaired after smoking marijuana. They work harder and more happily, they say, but they get less done—an acute effect found in this study.

Vitamin E Fails To Ease Angina In Toronto Trial

Medical Tribune World Service

TORONTO—The controversial claim that a majority of patients with anginn pectoris benefit from vitamin E therapy is not supported by results of a randomized, double-blind trial conducted here by University of Toronto investigators.

The study produced no "statistically convincing evidence" that patients who receive large doses of vitamin E fare any better than those who receive a placebo, according to Dr. Terence W. Anderson and coinvestigator D. B. William Reid, of the School of Hygiene.

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INSIDE THIS ISSUE

A Cure You Wouldn't Think Of: Noise for a Mouse Hangover

Medical Tribune Report

EAST LANSING, MICH.—There may be people who have had big heads who think it shouldn't happen to a mouse, but exposing the animal to intermittent noise during alcohol withdrawal will hasten recovery from symptoms.

Auditory stimulation enhances the development of inhibitory mechanisms, with resulting physiologic adaptation, two investigators from the University of Georgia School of Pharmacy reported here.

In experiments conducted by C. Phil Comer III and W. B. Hurrlan, Ph.D., mice of the CF-1 strain were made alcohol-dependent and then subjected to a "noise

test" to assess the severity of the acute withdrawal reaction.

Such alcohol-dependent mice are susceptible to sound-induced seizure for hours after they go on the wagon, Mr. Comer said in describing study findings to the fall meeting of the American Society for Pharmacology and Experimental Therapeutics held at Michigan State University.

Specifically, an initial startle response is followed by a short blind run, the mouse falls on its side in clonic convulsions, and it may show tonic flexion and extension.

This reaction—which the investigators term "identical in all respects" to audio-

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Long Flat EEG, Patient on Respirator Is Dead

Medical Tribune World Service

BARCELONA, SPAIN—If, in an unconscious patient who cannot breathe on his own, the brain registers no EEG activity, the likelihood is that he is irrevocably dead, said Dr. Benjamin Boshes, chairman of the Department of Neurology, Northwestern University Medical School, Chicago.

"A patient coming in totally unresponsive, requiring a respirator to sustain life, with flat EEG, stands a very high chance of being dead within 24 to 48 hours, provided there is no sedative drug intoxication," Dr. Boshes said.

"He will be equally dead if that decision is made 12 hours after the first flat EEG or after six hours. The question has been raised as to the likelihood of his being irrevocably dead if the decision is made after one hour, but much more data are needed to make this sure.

"The safest procedure at this point in our knowledge is to wait for at least six hours, and if the EEG is still flat for 30 minutes and drug intoxication and hypothermia have been ruled out, this patient has no chance of survival.

"It would be a kindness to the family and to the house staff to declare the patient dead. Then the respirator may be turned off. Such a patient would have fresh, viable organs to help a needy recipient. However, such a patient must be declared legally dead by a physician who understands all of these criteria. That person would be in no way connected at the time with any phase of the transplant procedure."

Dr. Boshes was reporting on a two-year study, "Cerebral Death," at the 10th International Congress of Neurology.

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To Catch Up With What's New on "Opportunistic" Systemic Mycoses Infections, Read Dr. Utz' IN CONSULTATION, Pg. 8

No Evidence That DDT Increases Liver Cancer

Medical Tribune World Service

AUCKLAND, NEW ZEALAND—There is no evidence that exposure of large numbers of persons to DDT for more than 30 years, and of the whole world population for nearly 20 years, has produced any part of the increase in liver cancer that was once feared, according to the Australian Nobelist Sir Macfarlane Burnet.

Giving this year's Sir Douglas Robb lecture at Auckland University, he also said that apart from an apparent rise in leukemia—probably due to better diagnosis—and the massive rise in lung cancer, there has been no significant increase in any of the major forms of cancer since the beginning of the century.

The belief that small doses of radiation could cause leukemia was based on the assumption that the cell damage was irreversible, he said, but this has now been disproved. Consequently, there is no justification for ascribing any significant proportion of leukemia or any other cancer to natural ionizing radiation, he said.

Recent evidence indicates that there is a threshold below which radiation has no effect, Sir Macfarlane declared.

His own view, he explained, is that cancer is a side effect of the evolutionary process and a means of regulating the life span of the species.

Even in the case of lung cancer, all the figures available indicate that age is just as important as cigarettes in determining the incidence of the disease, he stated.

A characteristic of old age is that it is a time when a considerable number of diseases became conspicuous, and cancer is the most important of them, Sir Macfarlane observed.

Almost all the common cancers increase steadily with age, as do strokes and heart attacks, he noted, adding that there is also evidence that the immune responses are heavily implicated in aging.

He believes that the thymus is the key organ in the process of aging.

Hospital Features Hotel Facilities

Genailer Clinic, which opened recently near Geneva, Switzerland, combines some features of both hotel and hospital. The idea, borrowed from Japan, is that a patient who requires extended care may have a member of the family stay with him. Facilities include an indoor pool and rooms with twin beds.

First Acupuncture Baby Delivered in Australia In 'Impressive' Procedure

Medical Tribune World Service

SYDNEY, AUSTRALIA—This country's first acupuncture baby, an 8-pound 12-ounce girl, was delivered uneventfully here at Mona Vale Hospital September 9 in a procedure that Dr. Harvey Turk, an obstetrician who was standing by in case of difficulties, found "very impressive."

The delivery was by Dean Rainer, a lay acupuncturist who has been practicing for five years since receiving training in Hong Kong.

"It was incredible," Dr. Turk commented. "Whenever there were contractions, Mr. Rainer twiddled his needles and the patient was out of pain."

A leading Sydney gynecologist, Prof. Derrick Llewellyn-Jones, welcomed the news of the event.

"I think acupuncture deliveries will become more common in Australia now," he said. "I think this will be a good thing. It is an excellent way of delivering a baby and has many advantages over drugs."

Low Insulin Secretion Related To Defect in Beta-Cell Signal

Medical Tribune World Service

BRUSSELS—Low insulin secretion seems to be common to prediabetes and diabetes and to be the result of defective initiation or transmission of a glucose insulin-releasing signal to the beta cell, the eighth Diabetes Congress was told here.

Presenting his findings in the Solomon A. Berson memorial lecture, Dr. Rolf Luft, of Karolinska Hospital, Stockholm, said this view carries at least two important implications:

- Further characterization of the cellular mechanisms in the defect of beta-cell receptor sensitivity or affinity for glucose may facilitate the development of pharmacologic agents.
- The possibility of preventing the metabolic consequences of insulin deficiency becomes a more realistic aim.

Dr. Luft said his team's work points to a cybernetic system governing glucose-stimulated insulin release. The glucose acts on a beta-cell membrane receptor to produce an insulinogenic signal, he said, but just how this signal is transmitted is not yet clear. Cyclic AMP is probably operative at some point in the process, he said.

Dutch MDs Raise Fees

Medical Tribune World Service

THE HAGUE—Consultation fees chargeable by general practitioners to private patients have been raised to 13.75 guilders (U.S. $5.08) for office visits and 20.5 (U.S. $7.60) for house calls.

New Virus Is Speculated On In Leukoencephalitis Study

Medical Tribune World Service

MOBIOKA, JAPAN—Progressive multifocal leukoencephalitis (PML), of which the number of cases does not exceed five in Japan and perhaps 100 in the whole world, is known to be a slow virus infection. However, virologic research in this disease is still in an early stage.

Results of research on PML were reported by the Bacteriology Department of Kyushu University to the 14th Clinical Virology Discussion Group.

Dr. W. Amako reported that (1) the PML virus is perhaps a new species differing from the already known papovavirus; (2) perhaps PML develops against a background of other diseases, such as leukemia, Hodgkin's disease; and (3) perhaps PML exists as a subclinical infection.

Male Patient Had PML

A male patient aged 46 admitted to the Neurology Department of the Kyushu University Hospital in July, 1970, was diagnosed as having a case of PML.

When the patient died in September, 1970, no formalin was used, but the body was stored in a refrigeration chamber, Dr. Amako said. The Pathology Department removed half the patient's brain and carried out a virologic examination.

This revealed scattered pathologic changes in the white matter, according to Dr. Amako, and when these were examined by electron microscope, virus particles about 40 millimicrons in size were discovered inside the nuclei of the glial cells. He said that the virus, in view of its negative staining and particle microstructure, belonged to the Papovavirus genus.

Since it is impossible to identify the species of a virus simply from its morphology, Dr. Amako said the investigators effected a microagglutination reaction under the electron microscope of the virus removed from the PML patient's brain, and from serum taken before death, and investigated the similarities and differences of PML virus from known papovavirus.

The method consisted of mixing the serum and the PML virus obtained from the brain, leaving it to stand at room temperature for 30 minutes, centrifuging it at 20,000 rpm for 30 minutes, and observing the sediment by the negative staining method: if an antigen-antibody occurred, a large conglomeration of agglutinated virus would be present.

Since this showed anti-PML virus antibody to be present in the serum, the serum was then reacted with SV_{40} polyomavirus and human papilloma virus, but no reaction occurred with these known viruses, Dr. Amako said.

On this basis he has concluded that this is perhaps a new virus that differs from known papovaviruses.

Cholera Vaccine Ineffective Unless the Disease Is Endemic

Medical Tribune World Service

JERUSALEM—Most physicians hold the cholera vaccine in such little esteem that they "take it with a fountain pen"—i.e., they simply testify that they have taken it, without actually doing so. This emerged from an open discussion about the effectiveness of the vaccine among physicians and bacteriologists at the first International Congress on Bacteriology.

Not one of the 200 physicians and bacteriologists in the hall rose to defend the vaccine. One physician held that the "vigorous application of soap and water and other sanitary precautions" would prove more effective. However, it was admitted that the vaccine is effective in areas where cholera is endemic.

news index

CLINICAL NEWS NOTE: *"As alcohol is released from the stomach it is readily absorbed from the gut; this alcohol is then metabolized in the liver, producing acetate, which circulates back to the stomach, inhibiting gastric emptying. Thus, alcohol absorption is controlled by its own metabolism."* (Dr. C. D. Eskelson; see page 38.)

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Lawyers and Doctors: Friends or Foes?

By Neil L. Chayet
Members of the bar, Massachusetts and District of Columbia

"Take a lawyer to lunch today!" You would probably no sooner take a lawyer to lunch than you would your mother-in-law. Jokes about lawyers abound at medical society meetings. Each new press release about lawyers mired in Watergate brings a self-satisfied glow to the hearts of doctors throughout the land, and never before have relationships between our professions been less cordial.

This column will look at some of the reasons for the continuing feud, provide some tips which will help you understand what makes law and lawyers tick, and perhaps turn apprehension and misunderstanding into a friendly—and very useful—relationship.

Doctors and lawyers are very different people, but the goal of each profession is much the same—to make the world a more tolerable place in which to live. The professions differ in their demeanor and their disposition, in their tools, in their ways of teaching and learning, in their approach to problems, and in their ways of practice. These differences, together with the fact that dealing with a lawyer may cost time and money or both, account for many of the problems. And the fact that many lawyers who find their practices cut back because of no-fault auto legislation have taken up the specialty of medical malpractice suits has not helped very much either.

The process by which problems are solved also causes much friction, and is responsible for most of the ill will from the moment the lawyer enters law school. He is nurtured in controversy, he learns by the case method—the Socratic method, as it is often called—he debates, argues, cajoles, and reassures throughout his career. You, the physician, on the other hand, learn surgery by lecture, textbook, and clinical practice; your relationship with other physicians is usually cooperative; the spirit of adverseness is unknown. And it is important to remember that the adversary process is much more a method of seeking an end to disputes than it is a seeking of truth. It is crude, but we have been able to find no other method that works as well, and though truth may not in fact be obtained, at least a court trial has declared an official truth and society accepts it, if only because nothing better is available.

Knowing a few basic principles is helpful. The lawyer can compel your presence in his forum, the court room, by a subpoena and a witness fee given (usually $3 or $4). He can ask you what you observed and what you did, but he cannot ask you for your opinion. This is the difference between an ordinary witness and an expert witness, and many lawyers will convert an ordinary witness into an expert witness. Unless you have been paid an expert witness fee ($150 or more) to form an opinion, you should not give one.

New Problems May Arise

Once you do assume the role of an expert witness, however, a new set of problems of communication may arise. For example, a frequent question is: "Doctor, did this accident cause the injury complained of?" On the surface, this is a simple question, of interest to both you and the lawyer, so you innocently begin your answer. The arguing begins almost immediately because no one really understands what the other is talking about.

Professor Small cites the classic case of the coal miner who was severely injured in an explosion, suffering two skull fractures, burns, bruises, fractures of both arms, and shock. He lay unconscious for 15 days, and on the 16th day he died. His doctors were asked at a Workmen's Compensation hearing what caused death. "Blocked bowels," they answered, and steadfastly refused to offer an opinion that anything else was the cause of death. When pushed further, two of them specifically said that the explosion had nothing to do with the death.

The problem is that the doctor is interested in etiology, while the lawyer focuses on the human event which precipitated the initial injury which led to death. The lawyer will also use the word "cause" when he means hasten or aggravate, as the law will also compensate a victim's family if his death had been hastened by the wrongful act of another, even though he may have had many underlying medical problems to begin with. Frequently, the doctor gets quite upset at the question "Did the accident cause the death?" and answers, "Of course not," citing a myriad of underlying medical problems as the cause of death.

Other problems arise over the words possible and probable. Lawyers function within a setting that revolves around the burden of proof. In a criminal trial, for example, a fact must be proved "beyond a reasonable doubt." In a civil trial, however, it need only be proved by a preponderance of the evidence, hence the terminology: "Doctor, can you state with reasonable medical certainty?" Mere possibilities are not admissible; so when the doctor says it is probable, the opposing lawyer will try to drive him back to possibilities; if the doctor says it is only possible, the other lawyer will try and push the other way. The real answer lies in being well prepared, knowing what the lawyer is seeking to do and why, standing firm, being consistent, and, most important, keeping your cool.

Remember also that, in the courtroom, credibility, demeanor, and just "looking good" are important, and if a lawyer is having problems with you because you are too well prepared and are just not supporting his case, he may change his tactics and try to make you lose your cool. Too often, the following will take place:

Lawyer: "Doctor, are you being paid to appear here today?"

Doctor (in a very small voice and after hesitation: "Yes."

Lawyer: "How much?"

Doctor (in a smaller voice): "$150."

Lawyer (loudly): "$150! For one hour's testimony? No further questions."

For the doctor who is prepared for such tactics the colloquy will be very different.

Lawyer: "Doctor, are you being paid to appear here today?"

Doctor (loudly and firmly): "I certainly am—$150, and it doesn't even begin to compensate me for the time I've spent preparing for today and waiting around to be called."

By the way, you should not have to wait around a courtroom for hours to be called. If you speak up, you can usually be put on out of turn and allowed to return to your work.

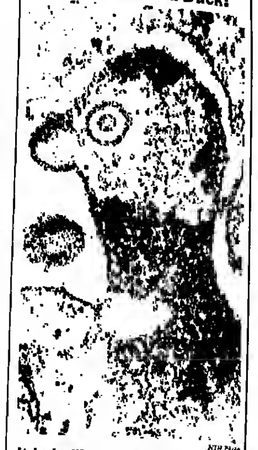
Fee Taking Problematic

The way in which fees are taken has also caused much misunderstanding. The lawyer often functions on a contingency—that is, if he loses he receives nothing; if he wins he may receive as much as 30-40 per cent of the verdict. He has difficulty in understanding why the doctor should not function similarly. There is nothing improper about asking for payment in advance of your testimony. I would rather pay a good doctor in advance and have his testimony than have him refuse to assist because he was not paid by the last lawyer for whom he testified.

Lastly, it is a fact that lawyers do sue doctors for malpractice, and that they do function on a contingent fee basis, which is one more reason why they try to get the most money for their clients. When I was handling many of these cases, the contingent fee system was a great safeguard, for no lawyer worth his salt will take a frivolous malpractice case. They are very rarely settled out of court and often involve as much as five years' work; so the lawyer, if for no other reason than economic reality, will screen these cases very carefully. In addition, the commission on malpractice did not support the charge of many doctors that lawyers are the major reason for the current volume of malpractice cases, and that an injured or angry patient is the major contributing factor.

Let us explore ways that our professions can communicate and understand, for together we hold the keys to better lives for all.

No, It's Not a Duck!



It looks like a duck, but it is actually a portion of the nucleus of a human cell infected with herpes virus and consequently distorted. The microphotograph is from a National Institutes of Health research project.

NHLI Plans to Give Grants For Lung-Related Research

Medical Tribune Report

Bethesda, Md.—The National Heart and Lung Institute is giving grants on a competitive basis to young scientists and physicians for pulmonary or lung-related research of their own design.

Applicants must be under 35, and applications must be turned in by December 1. Further information may be obtained from Jay Moskowitz, Ph.D., acting chief, Special Programs and Resources Branch, Division of Lung Diseases, National Heart and Lung Institute, Bethesda, Md., 20014.

"Double first cousins are indeed more closely related than first cousins. It appears that they are related twice as closely as first cousins or one half as closely as children of a sib-sib union."
—"Problems/Solutions" in *Postgraduate Medicine.*

And the thing about sib-sib unions is that they keep the sibs off the streets at night.

(Regular beats Immateria Medica, page 39.)

Major Complications Absent During 4,000 Colonoscopies

Medical Tribune Report

New York—The usefulness and safety of colonoscopy in diagnosing lesions throughout the length of the colon is limited only by the paucity of fully-trained endoscopists.

Dr. William I. Wolff, Mount Sinai School of Medicine, reported that there were no significant complications in the 4,000 colonoscopies performed in his unit since June, 1969. There were only two complications, both managed conservatively and successfully, during removal of more than 600 colonic polyps larger than 0.5 cm. in diameter.

Perforation and hemorrhage may occur in inexpert hands, Dr. Wolff stated, but safety and success are increasingly the rule. With the colonoscope, direct visualization of the colon has been extended from the first 15-25 cm. negotiable with the rigid sigmoidoscope to successful viewing up to the ileocecal junction in 95 per cent of patients.

Valued in Equivocal Situations

The instrument's most important use may be in early cancer diagnosis, when resection is most likely to be successful. It is also valuable in equivocal situations that cannot be clarified by x-ray and sigmoidoscope and in polypectomy above the sigmoid without using anesthesia or abdominal surgery.

Average hospital stay is two and a half days, much of it spent in preparing the bowel. A liquid diet is used the day before, and most patients are premedicated.

The colonoscope provides a clear diagnosis when x-ray studies are negative and symptoms positive, when x-ray suggests carcinoma above the sigmoid, and to determine the cause of overt or occult bleeding. Tissue specimens are easily obtained when malignancy is suspected; known or suspected polyps, both benign and malignant, can be removed through the device, and the efficacy of medical treatment for inflammatory disease can be fully observed. The colonoscope is also useful in follow-up after cancer resection; as it becomes increasingly available, it will also become more widespread as a screening device.

Information obtained through the colonoscope, Dr. Wolff noted, obviates unnecessary surgery when malignancy has been diagnosed by less precise techniques and expedites it when carcinoma is found.

An absolute contraindication for its use, he cautioned, is an inadequately cleansed bowel, which can lead to perforation or a missed lesion. Other contraindications are inflammatory bowel disease at an acute stage, such as fulminating ulcerative colitis, active granulomatous colitis, or acute diverticulitis. Leak from a fistula or possible postoperative perforation are also contraindications.

Dr. Wolff presented his findings to the second National Conference on Cancer of the Colon and Rectum sponsored by the American Cancer Society.

Newborns Screened for Hearing Loss

The automated "crib-o-gram" system, developed by Dr. F. Blair Simmons and in use at Stanford University Medical Center, detects infant movement in the crib and records any changes when a test sound is emitted. Physicians can judge whether an infant is deaf from its responses to the test sounds.

Australian MDs Launch Freedom Fund to Fight Nationalized Medicine

Medical Tribune World Service

Canberra—The Australian Medical Association has launched a $1,000,000 "Freedom Fund" to fight socialized medicine.

The 15,000 members of the association have been sent a letter declaring:

"The professional independence and freedom of the medical profession is being insidiously eroded. Interference by governments in the relationship between doctor and patient has been increasing steadily, to the detriment of both. Now, with the process of creeping nationalization apparently poised for rapid acceleration, a crisis point has been reached."

Meanwhile, the Federal Cabinet has taken a major step toward establishing the controversial national health scheme. It decided to set up an Australian Health Insurance Commission to administer a fund that would take over an estimated two-thirds of the health insurance now handled by private funds.

Under the Government's health plan, all persons except those with the highest or lowest incomes would contribute 1.35 per cent of their taxable incomes to the insurance fund. They would receive free public-ward hospital coverage and medical coverage for at least 85 per cent of doctors' bills.

Man Tied to Fever Spread

Medical Tribune World Service

Geneva, Switzerland—Man-made pollution is helping to contribute to the spread of yellow fever in West Africa and dengue hemorrhagic fever in Southeast Asia, according to the World Health Organization.

Both diseases are transmitted by the Aedes aegypti mosquito, one of whose favorite breeding places is in used car tires filled with rainwater.

(SEE PRECEDING PAGE FOR SWEEPSTAKES DETAILS)

On systemic mycoses infections

The Consultant

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Richmond.

"... systemic mycoses are accompanied by an impressive case fatality rate."

THE SYSTEMIC MYCOSES have frequently been considered rare and exotic illnesses, occurring so sporadically that their recognition seems hardly important. Although this attitude may persist in some places even today, I believe there is increasing recognition of the fact that these infections are presenting major problems in patients who are otherwise recovering satisfactorily from other serious diseases (leukemia, Hodgkin's disease, lymphoma) or are doing reasonably well following a dramatic and otherwise successful therapeutic maneuver (renal or heart transplant).

Secondly, the occurrence of such infections as "opportunists" has led to an increasing demand and expectation of microbiology laboratories and of attending physicians in making the proper diagnosis at the earliest date. Newer cultural media have been appearing from time to time. Attention has been directed toward diagnosing at least some fungal infections by detection of the fungal antigen in body tissues, such as cerebrospinal fluid or blood.

Skin and serologic tests for their diagnosis are being regularly and critically evaluated.

Thirdly, established therapeutic agents for a number of the systemic mycoses are either of such limited efficacy or of such extraordinary toxicity that a search continues for newer and better drugs. Notice of these appears frequently in the literature.

Fourthly, there is widespread recognition that such diseases are unreported in *Morbidity and Mortality Reports*, that they are not reportable in most states, and that our knowledge of the epidemiology and frequency of such diseases is fragmentary and rudimentary.

What is the relative importance of the systemic mycoses among infectious diseases?

It seems clear from closed as well as other population groups that viral infections are the commonest causes of infectious diseases in men and women of all ages. Among hospitalized patients there is also little question that bacterial disease is more frequently encountered. However, the systemic mycoses which develop in general population groups or in hospitalized patients tend to have an extraordinary severity and to be accompanied by an impressive case fatality rate.

The mycoses are currently and modishly divided into "opportunistic infections" and the others which seem to lack a certain glamour. Those which seem to occur under particular circumstances related to such things as corticoid, immunosuppressive, or antibacterial therapy or other illnesses include candidosis, aspergillosis, cryptococcosis, and phycomycosis. To the extent that nocardiosis is mentioned in relation to fungal infections, it is certainly also opportunistic. The other infections which seem to occur year in and year out, in various geographical areas, in this and other countries, regardless of such predisposing factors, are blastomycosis, histoplasmosis, coccidioidomycosis, sporotrichosis, and paracoccidioidomycosis.

What are the specific characteristics of systemic mycotic diseases that should alert the physician to such clinical diagnosis?

I suppose the first clue is an infectious disease which seems to be banging on, has not resolved, has not responded to antibacterial therapy, and which appears to have a chronic or subacute course. An example of this would be pneumonia. It is a characteristic of virtually all the systemic mycoses that they begin with a pulmonary lesion either clinically or subclinically.

From such a focus the disease then disseminates in a fashion such that the diagnosis may be suggested by the other presenting finding. For example, a lymphocytic meningitis, again of chronic nature, should certainly suggest cryptococcosis. A large warty skin lesion, especially on the exposed parts of the body, should bring up the question of blastomycosis. A finger lesion that is accompanied by reddened areas centrally along the path of the lymphatics certainly suggests sporotrichosis. Bone lesions that are not accompanied by signs of acute sepsis should suggest blastomycosis or coccidioidomycosis. Fortunately, dual infections are rare.

Once suspected, what should be the logical sequence in confirming the diagnosis of systemic mycoses?

Really no different from that with bacterial disease. For virtually all of the systemic mycoses the physician must order the proper specimens to the laboratory so that the causative fungus can be isolated. Such specimens include fresh early-morning sputum, freshly voided urine specimens, abnormal cerebrospinal fluid, blood, and bone marrow specimens, and, when indicated, lymph node or liver biopsy material. Under certain circumstances such direct preparations as the Wright stain of the sputum, KOH of pus, and India ink of cerebrospinal fluid may give a diagnosis even before the fungus can be cultured from such specimens.

> **Next In Consultation**
>
> DR. FRANK E. STINCHFIELD, Professor and Chairman, Department of Orthopedics, Columbia University College of Physicians and Surgeons, New York.
>
> ... will discuss changes he has seen in orthopedic surgery and answer questions on the possibility of knee replacement, selection of patients, and the problems of complications.

What are the basic guidelines in the treatment of the systemic mycoses?

The first, major, and important mode of therapy for these infections is that of a thoughtful physician's attention to the complaints of his patient. A cough or chest pain that disturbs the patient's sleep at night should not be unworthy of his physician's immediate concern and attention. The infection of the lung should not override any consideration of the patient's respiration and of whether he needs ventilatory assistance. It is all well and good to culture urine and prostatic massage material from the patient with blastomycosis, but it is even more important to prescribe a scrotal support for epididymitis and sitz baths for prostatitis.

The second major aspect of therapy is surgery. A loculated abscess must be drained for therapeutic as well as diagnostic reasons. Chronically inflamed and relatively avascular fibrotic or inflammatory tissue, as seen in patients with actinomycosis, must be resected. The lethargy in a meningitis patient may not be related to the fungus in the cerebrospinal fluid, but instead to obstruction of his ventricles, so that a ventriculojugular shunt or an Ommaya reservoir is of critical importance.

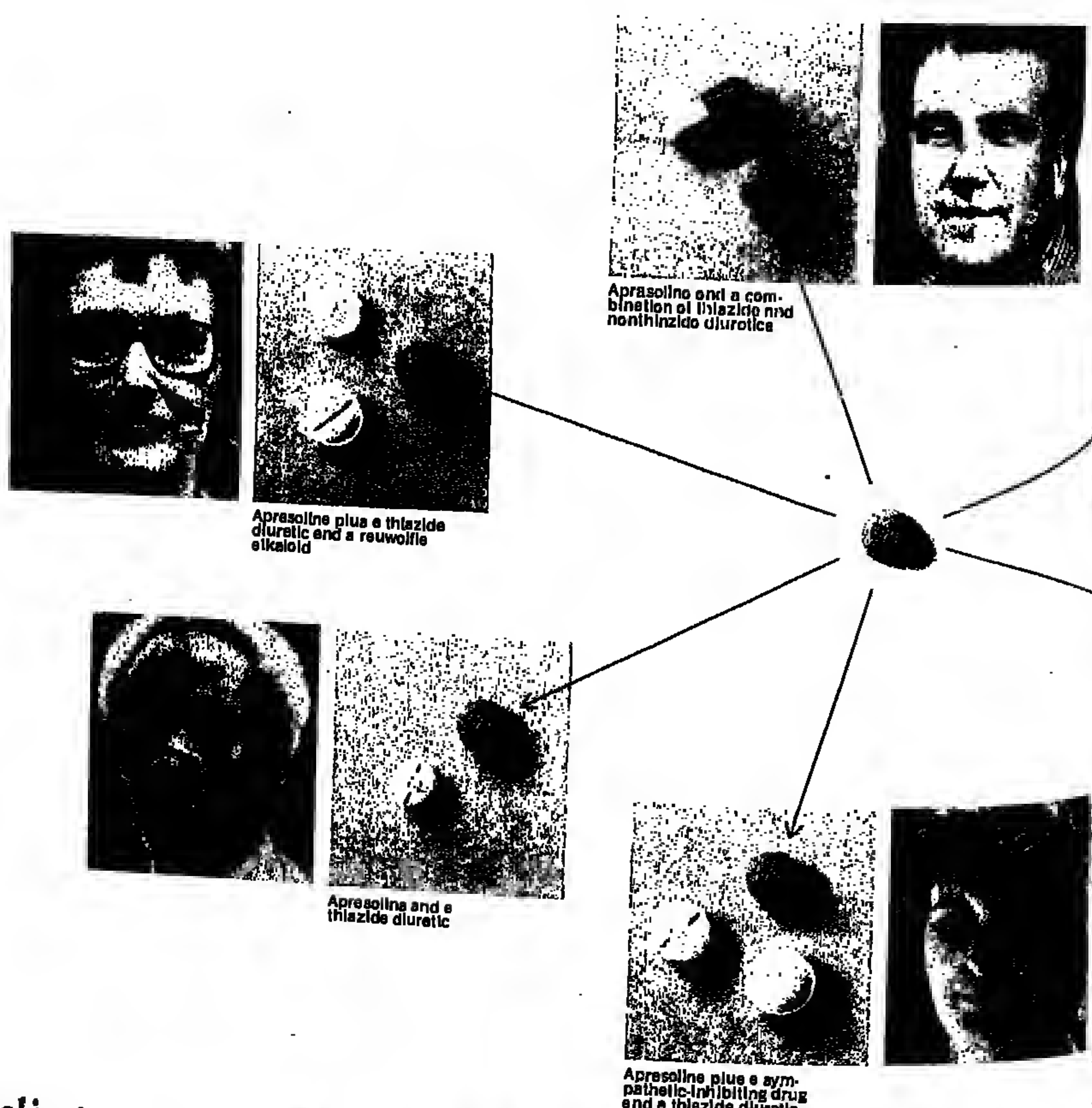
Third, and probably most important, the correct antimicrobic agent must be selected, used carefully and expeditiously, and the side effects conscientiously looked for. The recommended drugs for particular fungal infections are suggested in the accompanying table.

The Systemic Mycoses: Disease and Recommended Drug

	First Choice	Second Choice
Actinomycosis	Penicillin	Clindamycin
Nocardiosis	Sulfonamide	Ampicillin or tetracycline
Histoplasmosis	Amphotericin B	Sulfonamide
Blastomycosis	Amphotericin B	2-Hydroxystilbamidine
Sporotrichosis	Potassium iodide	Amphotericin B
Candidosis	Amphotericin B	Flucytosine
Cryptococcosis	Amphotericin B	Flucytosine
Coccidioidomycosis	Amphotericin B	No other drug
Aspergillosis	Amphotericin B	No other drug
Mucormycosis	Amphotericin B	No other drug

What progress is being made in antifungal therapy?

One of the most fascinating aspects of fungal therapy—being developed by workers in St. Louis, notably, but elsewhere as well—is combined treatment. Such is based on both facts and hypothesis: Fact 1 is that amphotericin B is known to attach to specific steroids, notably ergosterol, in fungal cell membranes. Fact 2 is that flucytosine appears to interfere with nucleic acid synthesis at one of four or five positions. Hypothesis 1 is that amphotericin B, by attaching to the cell membrane, renders it more permeable to flucytosine. Fact 3 is that additive or synergistic effects have been demonstrated both in vitro and in animal infections. These facts and the hypothesis have led to a cautious trial of such combined therapy for cryptococcal meningitis.

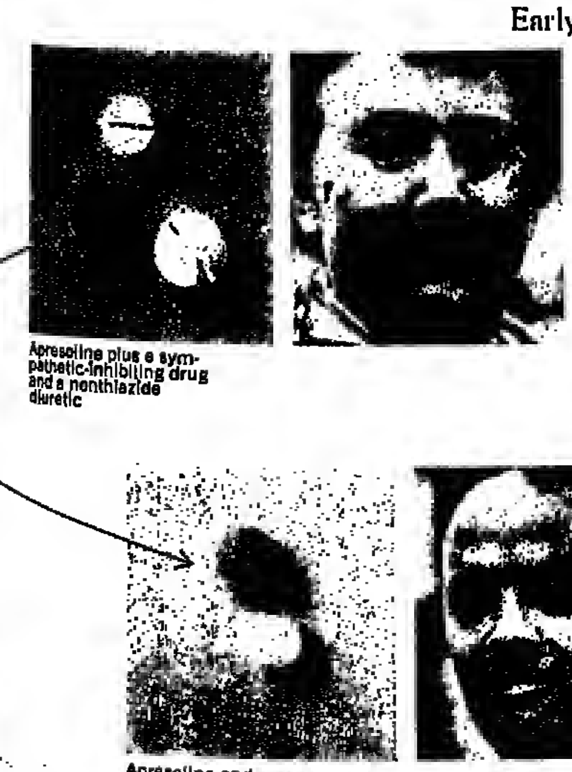


Apresoline and a combination of thiazide and nonthiazide diuretics

Apresoline plus a thiazide diuretic and a rauwolfia alkaloid

Apresoline and a thiazide diuretic

Apresoline plus a sympathetic-inhibiting drug and a thiazide diuretic



Apresoline plus a sympathetic-inhibiting drug and a nonthiazide diuretic

Apresoline and a nonthiazide diuretic

Unthought-Of Cure: Intermittent Noise For Mouse Hangover

Continued from page 1

sensitization seizures—is evoked by 60 seconds of exposure to sound, such as that of a bell. The percentage of tested mice that experience clonic-tonic seizures provides an objective measure for determining the severity of withdrawal reaction.

As human boozers might predict, the incidence of sound-induced seizure peaks at 12 hours following withdrawal. More than three-fourths of the mice experienced seizures at that point. About 50 per cent responded with seizures 20 hours after withdrawal, and the incidence did not begin to decline from this level until between the 30th and 35th hours.

But the pattern differed markedly for two groups of mice that were given the auditory stimulus at the sixth hour and again at the 12th hour following withdrawal. Less than half had seizures at the six-hour point, and an even smaller proportion (less than 25 per cent in one group) had them when tested at 12 hours. By hour 30, sound would induce seizure in less than 10 per cent.

Mice—like men—differ from each other, and the investigators discovered that mice of the CBA strain can undergo acute withdrawal from alcohol without going into the murine equivalent of the fantods when exposed to sudden sound or picked up by the tail (a maneuver that causes convulsions of varying severity in alcohol-dependent CF-1 mice).

Effects Are Masked

Further testing of these apparent stalwarts, however, demonstrated that effects are masked rather than absent. Although such mice were as immune to sound-induced seizure as control animals at 13 and 20 hours after withdrawal, if the alcoholics were given reserpine at the 20th hour some 83 per cent of them developed seizures in response to noise. None of the controls did so.

Administration of reserpine also unmasked chronic dependance on alcohol in the seizure-prone CF-1 alcoholics. These animals seemed to be over the hump nine days after alcohol withdrawal, since none had seizures on exposure to noise. But reserpine on the 10th day caused 10 per cent to experience seizures when subjected to noise. The effect became even more striking 20 hours after the drug was given, when 41 per cent responded to noise with seizures.

Study findings suggest, the investigators conclude, that physiologic adaptation following acute alcohol withdrawal "results from development of passive inhibitory mechanisms, a process which may be hastened by intermittent sensory stimulation to produce a more active inhibitory process." Both active and passive phases of such adaptation are blocked by reserpine.

Caution Notice Ordered For 'Morning-After Pill'

Medical Tribune Report

WASHINGTON—The Food and Drug Administration has concluded that diethylstilbestrol (DES) is effective for use as an emergency postcoital contraceptive but has ordered that a patient package insert be distributed to users of this so-called morning-after pill, warning patients of the side effects and risks of using the drug.

The FDA stated that it "does not consider the drug safe for routine or repeated contraceptive use because of the relatively large amounts of estrogen taken over a short period of time."

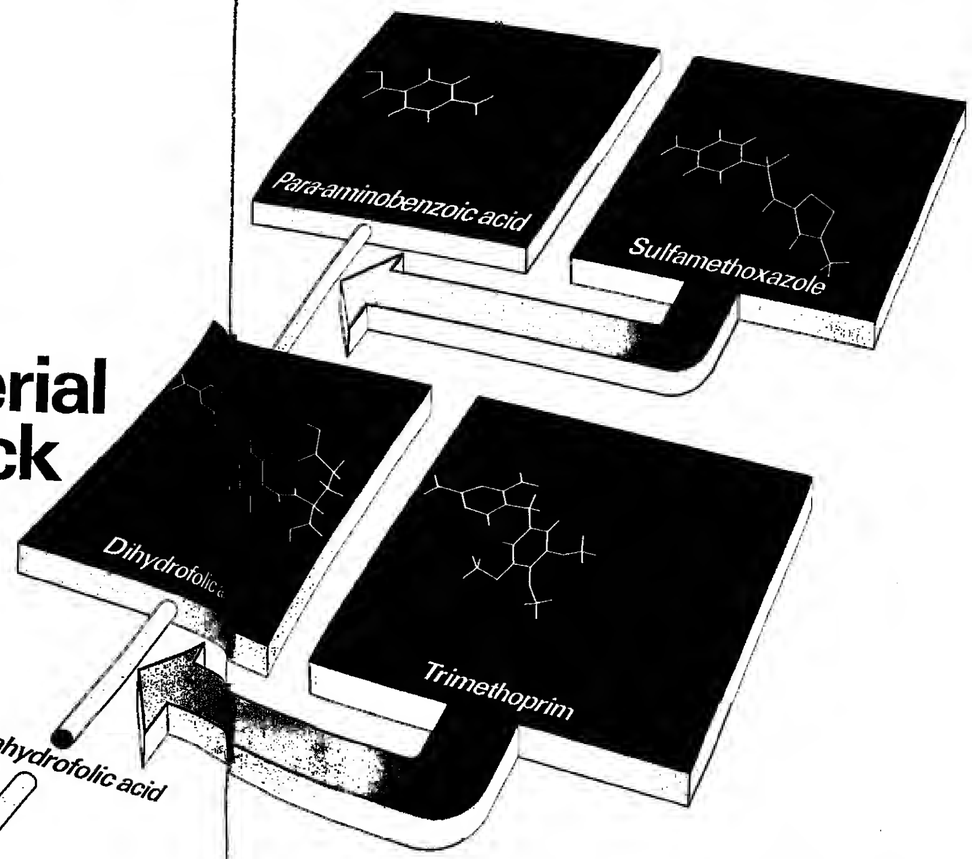
The patient package insert warns the user that if a pregnancy occurs despite the administration of the drug, she should consider undergoing an abortion because cancer of the vagina has been noted in some female children of women who consumed the drug during pregnancy.

ROCHE announces new BACTRIM™

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

a new type of antibacterial for a two-pronged attack against chronic urinary tract infections due to susceptible organisms

Bactrim is highly effective in the treatment of these infections—primarily pyelonephritis, pyelitis and cystitis—when due to susceptible organisms. This efficacy is related to the unique mode of action against bacteria (see illustration), an action that, in effect, makes Bactrim a new type of antibacterial.



Bactrim interrupts the life cycle of susceptible bacteria

Unique mode of action interrupts the life cycle at two important points, thereby impeding the production of nucleic acids and proteins essential to these bacteria. These consecutive interruptions occur because sulfamethoxazole and trimethoprim resemble naturally existing substrates. By competitive replacement of these substrates, they inhibit further synthesis.

Prescribing considerations

Clinical Limitations: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections. Not recommended for children under twelve.
Contraindications: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period.
Warnings and Precautions: Both sulfamethoxazole and trimethoprim have been reported to interfere with hematopoiesis. Complete blood counts should be done frequently. If a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued. Bactrim should be given with caution to patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. Maintain adequate fluid intake. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.
Adverse Effects: Among the most common side effects are nausea, vomiting, rash, leukopenia and elevations in SGOT and creatinine.

ROCHE

Excellent clinical response in chronic urinary tract infections even with obstructive complications

A multiclinic, double-blind study* of response to a ten-day course of therapy in 471† patients with chronic urinary tract infections demonstrated the superiority of Bactrim. On the 10th day after initiation of therapy, 91.7% (of 168 patients) showed significant bacteriological response to Bactrim, compared with 81.2% (of 144 patients) to trimethoprim and 64.5% (of 155 patients) to sulfamethoxazole. More than half of these patients had obstructive complications.

Excellent response maintained

Bactrim proved equally impressive in maintaining this bacteriological response. In the above study, after a ten-day course of therapy with Bactrim, 68.4% of patients with chronic urinary tract infections *maintained* response for up to 42 consecutive days, compared with 59.7% with trimethoprim and 44.4% with sulfamethoxazole. These results are particularly noteworthy considering the number of patients with obstructive complications—cases regarded as being notoriously difficult to treat.

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110
†4 patients not available for evaluation at day 10.

new BACTRIM™

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections

Before prescribing, please see complete product information on following page.

Virus May Trigger and Play Role in Multiple Sclerosis

Medical Tribune World Service

BARCELONA, SPAIN—A virus may not only trigger the chain of events leading to the development of multiple sclerosis but may also figure in the disease process itself, Dr. Hilary Koprowski, of the Wistar Institute, Philadelphia, told the 10th International Congress of Neurology here.

Dr. Koprowski based this view on two discoveries:

- The direct isolation of a virus from multiple sclerosis brain cells maintained in tissue culture.
- The demonstration of ultrastructurally similar if not identical nucleocapsids in brain cells obtained from early demyelinating lesions in a multiple sclerosis case.

Dr. Koprowski identified the virus as the 6/94 agent, a new member of the parainfluenza type 1 group. It differs from the HA2 and Seadai (HVJ) prototype viruses both serologically and in growth characteristics, he said.

It is much less cytocidal for cells in culture than either of the other two viruses, he said, and "can easily be used to establish a persistent type of infection of the cells."

Cells infected with the 6/94 agent, Dr. Koprowski reported, will hemadsorb guinea pig red blood cells when maintained at incubation temperature of 32° to 33° C. but not when grown at 37°.

"Subtle differences between the 6/94 and the Seadai viruses may also exist in the number of species of proteins and in patterns of various RNA components," he added.

May Cause Mild Infections

The Sendai and HA2 viruses have not been known to play a role in diseases of the central nervous system, he observed, but HA2 is a causative agent in relatively mild respiratory infections.

Dr. Koprowski stressed the point that lipids of parainfluenza viruses are mainly determined by the host cells in which the viruses are propagated; thus the viruses that bud from cells have characteristics that are dependent upon the types of cells in which they reproduce. "Moreover, the fact that multiple sclerosis correlates with certain antigen specificities may mean that it is possible that some individuals are genetically predisposed to react differently to an infection with a viral agent which in the rest of the population may cause only minor illnesses."

He cautioned that thus far there is, at best, only a hypothetical case for the role of 6/94 in multiple sclerosis, and noted that there is indirect evidence of the roles of other viral agents.

Citing the higher concentrations of antimeasles antibodies in the sera of multiple sclerosis patients, he said that "the presence of these antibodies, and antibodies directed against vaccinia viruses, in the central nervous system of multiple sclerosis patients may indicate such involvement."

Dr. Koprowski recommended "epidemiologic studies in high- and low-incidence areas, conducted along the patterns established for polio virus infections, as a means of elucidating the role of a virus in the etiology of multiple sclerosis."

In another paper presented at the conference, Dr. John Zabriskie, of Rockefeller University, New York, said that peripheral blood leukocytes from patients with multiple sclerosis show greater reactivity to human or rabbit brain basic protein antigens.

Leukocytes from normal subjects do not show evidence of cellular reactivity, Dr. Zabriskie said, and the degree of reactivity in the case of multiple sclerosis patients seems to depend on whether autologous or homologous serum is used.

Pancreatic Therapy Sought for Diabetics

Medical Tribune World Service

BRUSSELS—Therapy aimed at the beta cells of the pancreas may open the way to a brighter future for diabetics, Dr. George F. Cahill, Jr., Professor of Medicine at Harvard Medical School, said here in the J. P. Hoet memorial lecture at the eighth Diabetes Congress.

Research is now fanning out in three directions, he observed:

- Correction of an as yet hypothetical defect in these cells or their governors.
- Transplantation of the cells from either human beings or animals.
- A mechanical means of delivering insulin more closely resembling beta-cell activity.

Replacement of these cells, or at least their function, could offer patients a future free of the microvascular complications and accelerated atherosclerosis that now plague diabetics, said Dr. Cahill.

He described two approaches, developed in the United States, toward "the artificial pancreas." One uses a glucose-sensitive metal catalyst electrode capable of oxidizing the sugar and generating a proportional current. The other uses a glucose oxidase coupled to an oxygen electrode that registers the amount of the gas used in the reaction.

Blood Flow In the Eye

Bernard F. Hochheimer and Robert W. Flower, of the Johns Hopkins Applied Physics Laboratory, have developed a technique using a dye, indocyanine green, to permit detailed viewing of the blood flow in the choroid of the commonly pigmented human eye. Sodium fluorescein dye, when used with indocyanine green, provides ophthalmologists with simultaneous photographs of both retina and choroid (above). The choroidal vascular system provides much of the nutrition for the retina and all of that for the central macular region.

BCG Administered Orally Effective in Stimulating Tumor Immune Response

Medical Tribune World Service

SALZBURG, AUSTRIA—Oral administration of lyophilized BCG in an attempt to stimulate immune response in the area of a tumor has been tried at the Connaught Laboratories in Toronto, and the results suggest that this method is sometimes effective.

Dr. R. R. Falk, of the University of Toronto, described the work to the Joint European Assembly on Cytology and Cancer Prevention here.

Sixty patients with disseminated malignant melanoma or carcinoma of the gastrointestinal tract were given oral BCG over an 18-month period. They received 120 mg. at least weekly, the dose being decreased if there was objective regression.

Of 14 patients with disseminated melanoma, objective regression was noted in eight, Dr. Falk reported. The therapy was ineffective in patients with advanced hepatic metastases. All patients who responded with tumor regression showed enhanced reactivity to both tumor membrane antigens and BCG in in vitro tests.

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I. Scapegoats, Washington—and Doctors

One sadly notes how essential the scapegoat is to the Washington scene. Attention must be drawn to a clear pattern that has existed through several administrations—a pattern of making the physician the scapegoat for the real, pressing, and complex problems of public health. This Administration does not stand alone in respect to questionable behavior toward physicians, nor does government stand by itself; there are others who have participated in and fostered the scapegoating of the American physician. If the very real problems of public health were soluble by the sacrifice of the medical profession, one might have some understanding; but the fact is that they cannot contribute significantly to the solution of health care problems. Governmental attacks on physicians disrupt the physician-patient relationship, damaging the patients' interests; they have misled both political leaders and the American people in regard to the very real issues that must be faced and solved.

We know of no public health authority who has considered medicinal drugs—or, for that matter, narcotics—as a major public health problem. We know that virtually all consider alcohol and tobacco as two of the leading preventable causes of disease. We know of no evidence that a reduction in physicians' fees or lower cost of medications can for any significant period of time arrest the escalating cost of catastrophic disease or of hospital costs. We do know that adequate numbers of physicians and new medications have in the past reduced what would today have been an intolerable burden—the costs of care through preventative and curative medicine in acute and infectious disease, tuberculosis, psychiatric disorders, etc.

The selective efforts exercised by governmental agencies focusing headlines on minor issues are worse than nothing because they mislead the public as well as the profession and defer the day when real issues will be realistically examined, defined, and faced.

Terminology and Cancer

One of the penalties of ever-burgeoning science is the introduction of terms and phrases that are clear to the initiate but pose problems to the rest of us; the latest editions of dictionaries are turned in vain, and no ready reference is available.

One of the hot investigative areas current today is the effort to incriminate viruses as causes of human cancer, and repeatedly one reads of RNA viruses, type B particles. Presumably there are at least also type A and other particles. But what are they? It is comforting to learn from an editorial in an issue of the *Journal of the National Cancer Institute* that even experts have been confounded, and as recently as last year the statement was made that "confusion continues to surround the terminology used to categorize members of the RNA tumor virus group."

It turns out that when Bernhard used the electron microscope to study different types of mouse tumors, he described four different morphologic particle types that were present. Two types associated with mammary tumor he called A and B. The particle type related to mouse leukemia he called type C. There is also a type D particle, but that is a small DNA virus that is intranuclear in location.

At the time Bernhard reported his findings in 1960, hardly anything was known about these particles other than their shape. Today it is known that the type B particles induce mouse mammary tumors, so these particles are truly the infective virions (composed of the nucleic acid core—the *nucleoid*—surrounded by protein—the *capsid*). Type C particles are the virions that induce murine leukemia. There are niceties about the electron characteristics of B and C particles that permit their distinction from one another and also different views as to just when this distinction is to be made. Study of A particles has revealed two types, one of which is the precursor of B particles, the other having no known biological activity.

Of course, the intriguing element about all this is that for a number of years B-type particles have been found in high incidence in human milk from women known to be at high familial risk of mammary cancer. Work in Spiegelman's laboratory and elsewhere has added evidence that these particles may indeed be the cause of human cancer of the breast, but the crucial transmission experiment that demonstrated the neoplastic effect of B particles in the mouse is, of course, forbidden in man. Lower primates can be tested and persuasive proof may be forthcoming.

Vitamin E and Angina

Clinical Quote: "*There would appear to be two possible explanations for the failure of . . . double-blind trials to confirm the dramatic effects that have been reported by some authors. Either that vitamin E is of no value (and the favorable reports are due entirely to a combination of spontaneous remission and placebo effect) or that vitamin E has a small effect and spontaneous remissions and placebo effects make up the balance. . . . Scientific caution requires that the first explanation (no effect) be accepted until it is shown to be wrong.*" (Drs. T. W. Anderson and D. B. William Reid, U. of Toronto School of Hygiene; see page 1.)

"A lot of good those get-well cards did him!"

LETTERS TO TRIBUNE

On Vitamin C

In response to Dr. J. W. Meigs ("Letters to Tribune," September 26):

I am one of those unfortunate people who had to suffer severe colds through years, since childhood.

For the past three years, I have not had any colds, since I take routinely at least 2 Gm. of vitamin C, and at the first signs of a suspected cold I increase the dosage to at least 3 Gm. per day. The cold does not develop. I take vitamin C always after or during meals, not on an empty stomach.

NINA TOLL, M.D.
Middletown, Conn.

A Kick About Feet

In your August 22 issue you carried an entire section related to foot disorders in runners. The lead article regarded a talk given by Dr. George Sheehan, a cardiologist, regarding foot problems, before the California College of Podiatric Medicine. He was quoted as stating "90 per cent of doctors know nothing about the foot, and orthopedic surgeons have never helped."

Naturally, as an orthopedic surgeon, I differ with his opinion. I do not feel the need to defend my specialty nor go into a point-by-point discussion of the various issues raised in these articles. However, I am curious to know whether Dr. Sheehan's orthopedic colleagues think as highly of him as a cardiologist as he does of them.

HOWARD STURTZ, M.D.
Walnut Creek, Calif.

Accusing Finger

Your recent article (September 19) on microsurgery by Dr. Owens of Australia was most interesting.

However, it is not true that, as Dr. Owens said, "in the United States not one finger has been replaced." Drs. Harold E. Kleinert and Joseph E. Kutz are running a very fine microsurgery unit in Louisville, Ky. They have a series of replantations over many years to their credit. I, personally, was part of a replantation team that replaced an index finger.

KENNETH N. ADATTO, M.D.
New Orleans, La.

Rewriting Dr. DuVal

Referring to Dr. M. K. DuVal's proposal for redistribution of physicians (MEDICAL TRIBUNE, August 15), I would like to suggest that his speech might well have been given in somewhat the following manner:

For the past 150 years, the physicians and politicians of this nation have worked together (sometimes in discord and sometimes in harmony but nevertheless all working together) in an effort to achieve a proper balance of physicians to population. Certain laws and regulations, such as medical licensure and income taxation, have proven effective in causing physicians to locate in certain areas in which they might not otherwise locate but there is still too much freedom of choice allowed to the individual physician. The result is that we have a system in which some groups of people have plenty of medical care available while other groups have less or none.

For this reason, the system should be regulated and placement proscribed even more than it is at this time, and I, the wise one, should be in charge of the allocation and distribution of physicians. In fact, I offer this plan as an alternative to governmental intervention, because with governmental intervention there will be physician placement by a whole army of bureaucrats with inefficient overlapping of efforts, but with my system there will be accurate and efficient and proper placement of all physicians by one man, ME, The Dictator. (In that way, we avoid any governmental intervention.)

ROBERT S. JAGGARD, M.D.
Oelwein, Iowa

All in Favor Say 'Da'

In your recent article about the latest socialist outburst of Senator Kennedy, proposing peer review of doctors by pharmacists, he wonders, at the end, "whether we need five or more companies manufacturing identical products."

If we look at Russia's example, we could do without four of them. Only one, owned and operated by the Government, is needed. Also, following Russia's example, we could do without senators and millionaires.

SERGIO M. ACOSTA, M.D.
Elmhurst, Ill.

Acid Advice

The boric acid advice given by your dermatologic consultant in the July 25 issue is fraught with peril.

Your consultant advises compresses of boric acid as treatment of acute painful sunburn. Quite apart from the danger of keeping boric acid in the household, where it may inadvertently be ingested by children, boric acid is absorbed through traumatized skin and, applied repeatedly, may lead to cumulation and toxicity.

The 1971 A.M.A. Drug Evaluations describes boric acid as "of doubtful therapeutic value ... no place in modern dermatologic therapy ... no place in modern medicine."

JEAN D. LOCKHART, M.D.
Director, Department of Committees
American Academy of Pediatrics
Evanston, Ill.

Mechanical Thumb Joint Implanted

Wide World Photo

A team of surgeons at Cincinnati General Hospital have performed the first implant of an artificial thumb joint in a human recipient. The joint, fashioned from a cobalt alloy, was developed by surgeons and biomedical engineers at the University of Cincinnati. The patient is a 54-year-old man who lost the use of his thumb 10 years ago.

Pain May Be 'Game' Patients Play—But the Stakes Are High

Medical Tribune World Service

MONTREAL—In certain cases, pain may be viewed as one of the "games" patients play, C. Richard Chapmnn, Ph.D., Seattle, suggested at the annual meeting of the American Psychological Association here.

If so, it is a game wherein the stakes come high, he observed, because the total cost in the United States alone of pain-related health care, loss of productivity, compensation, and litigation is put at about $10 billion annually.

Some patients referred to the University of Washington pain clinic, he said, had spent more than $25,000 on health services, including up to 25 operations. One patient had had 42 interventions.

"A conspicuous characteristic of chronic pain problems, particularly those in which pain behavior greatly exceeds the evident tissue injury, is that conventional medical therapy tends to be consistently ineffectual," he commented.

"The physician very often errs in assuming that pain signifies underlying pathology," said Dr. Chapmnn, who is a Research Assistant Professor in the Departments of Anesthesiology, Psychology, and Psychiatry at the university.

Dr. Chapmnn said that something akin to a career identity may begin to emerge in long-term pain sufferers. Those who are experiencing role confusion may tend to find a life atyle of an invalid attractive.

"Diagnostic tests, surgeries, experimental drug therapies, professional referrals and consultations, and new prescriptions all contribute to the legitimization of the chronic pain patient's newly adopted code."

Techniques Like Acupuncture Cited In Pain Relief

from McGill University

► Ronald Melzack, Ph.D., of McGill University, cited hyperstimulation analgesia, trepanation, counterirritation, cupping, and scarification as techniques that probably work in ways similar to acupuncture.

Dr. Melznck, who is coauthor of the gate control theory of pain, said that, in any ense, the first step in explaining acupuncture is to drop the simple one-to-one relationship between stimulus and pain.

One suggestion that follows from his own work, he said, is that surgical intervention in controlling pain should not take place with respect to the central nervous system except to relieve terminal cancer patients.

Further work, he believes, will center on learning how to activate built-in inhibiting mechanisms in the C.N.S. and probably on finding drugs to do this.

We Hear Quiet, Not Noise

Medical Tribune World Service

PERTH, AUSTRALIA—We are no longer conscious of noise—we hear quiet instead, Prof. R. G. Barden, of Monash University, told the Australian and New Zealand Association for the Advancement of Science.

"The growing problem of noise has all the makings of an epidemic, and there is an urgent need to stop the creeping paralysis of rising noise levels," he said. "Noise is more than a quality-of-life problem; its serious effects could range from intense mental stress to hearing loss."

Motor Neurons React To Corticosteroids In Myasthenia Gravis

Medical Tribune World Service

EAST LANSING, MICH.—The dramatic improvement sometimes seen in myasthenia gravis patients treated with high doses of corticosteroids is probably related to their effects on motor neuron function, according to a group of New York investigators.

Certain glucocorticoids have a facilitating action on motor neuron function, they said, and continued: "The excitability of these cells in cats given a high-dose, short-term regimen of either triamcinolone, fludrocortisone, prednisolone, or methyl prednisolone was found remarkably heightened."

They reported to the American Society for Pharmacology and Experimental Therapeutics that the change in excitability was demonstrated by a large increase in the ability of these neurons to produce long-lasting afterdischarges in response to a single stimulation.

Dr. Walter F. Riker, Jr., chairman of the Department of Pharmacology at Cornell University Medical College, who delivered the report, said that the corticosteroid effect develops gradually with treatment and apparently involves changes in the entire neuron. This differs from the action of other antimyasthenia drugs, which affect only the membranes of the unmyelinated motor nerve endings, he said.

"This steroid effect could underlie the exacerbation of seizure disorders by these drugs," Dr. Riker commented, but the "neuronal action probably signals a beneficial effect of these drugs in depressed neuronal functioning, especially as represented by their salutory effect on myasthenia gravis."

Coauthors were Drs. Thomas Baker and Michiko Okamoto.

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55. KNDWLTDN, S. B., JR., M.D., 1245 Highland Avenue, Abington, Pa.
56. KDZIDI, STANLEY M., M.D., 6505 N. Leroy Avenue, Lincolnwood, Ill.
57. KRANER, JUSTIN F., M.D., 8515 Delmar Boulevard, St. Louis, Mo.
58. KURZON, ALVIN M., M.D., 836 N. 12th Street, Milwaukee, Wis.
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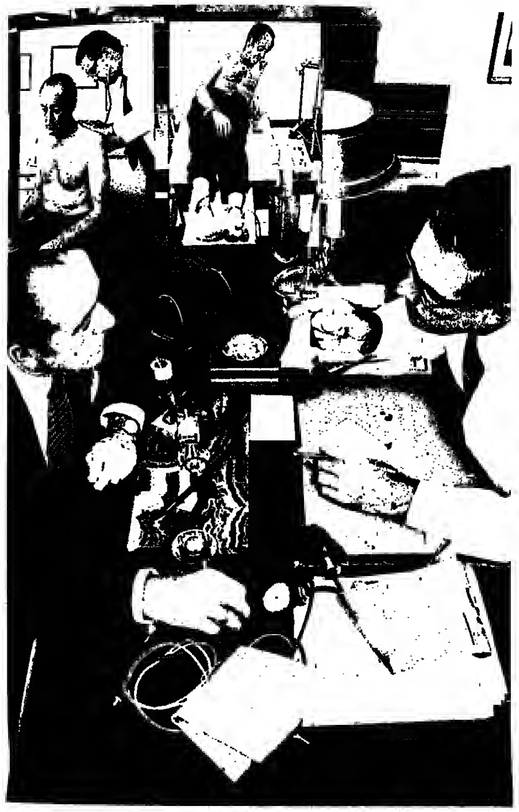
ENTER AS OFTEN AS YOU WISH!

The psychotherapeutic effect of Oral Valium® (diazepam)

in anxiety and somatic symptoms of excessive psychic tension

When a complete examination rules out organic disease, you may find that functional complaints involving the heart, stomach or colon—frequently seen in anxious patients overreacting to stress—are a result of excessive psychic tension. And if counseling alone does not suffice, you might consider Valium (diazepam) to help relieve these tension-induced symptoms. In general, it goes to work promptly, usually producing significant improvement within the first few days of therapy, although some patients may take longer to show a clear-cut response.

Available in three convenient tablet strengths—2 mg, 5 mg, 10 mg—Valium provides dosage flexibility for maximum patient benefit with a typical *t.i.d.* or *q.i.d.* regimen.



in anxiety with or without associated depressive symptoms in psychoneurotics

Valium (diazepam) can provide prompt relief when excessive anxiety and undue tension are a prominent part of the clinical picture. By relieving these symptoms, it can enhance response to therapy and add to the effectiveness of your total management of the psychoneurotic patient. Caution patients against driving or engaging in hazardous activities during therapy.

The recommended dosage is 2 to 10 mg, *b.i.d.* to *q.i.d.*, depending upon the severity of symptoms.

adjunctively in organic disorders complicated by undue psychic tension

Overly tense patients—particularly those with G.I. or cardiac disease—must be kept calm when undue tension and excessive anxiety aggravate their condition and interfere with therapy. Oral Valium can provide the desired response, generally without significantly adversely affecting respiratory, pulse or heart rates. It is used with most classes of primary medications such as cardiac glycosides, diuretics, vasodilators, anticholinergics and antacids, and is usually well tolerated; the most frequent side effects are drowsiness, fatigue and ataxia.

When nighttime anxiety precludes sleep, an *h.s.* dose added to the *t.i.d.* regimen can relieve the anxiety.

Please see the last page of this advertisement for complete prescribing information.

The psychotherapeutic effect of Injectable Valium® (diazepam)

prior to surgery

Injectable Valium (diazepam) can promptly calm the surgical patient by lessening the excessive anxiety and undue tension that may be associated with strange surroundings and disturbing procedures. And it can provide the added advantage of markedly diminishing recall of preoperative procedures.

The recommended dosage is 10 mg, I.M., administered one to two hours preoperatively. Injectable Valium should not be mixed or diluted with other drugs, solutions or fluids.

adjunctively prior to gastroscopy and esophagoscopy

Injectable Valium (diazepam) can be a valuable adjunct in allaying excessive anxiety when it accompanies such procedures. It calms the anxiety yet allows the patient to cooperate by responding to commands and following instructions. It is not recommended for bronchoscopy and laryngoscopy. Because of the possibility of laryngospasm, necessary countermeasures and resuscitative facilities should be immediately available.

Half an hour before gastroscopy or esophagoscopy, a 5 to 10-mg dose is administered I.M. or I.V.

prior to cardioversion

Through relief of undue anxiety and excessive tension, Injectable Valium (diazepam) can effectively calm the patient. Memory of the cardioversion procedure can be markedly diminished. Injectable Valium seldom significantly alters vital signs. Nevertheless, there have been infrequent reports of hypotension and rare reports of apnea and cardiac arrest. Resuscitative facilities should be immediately available.

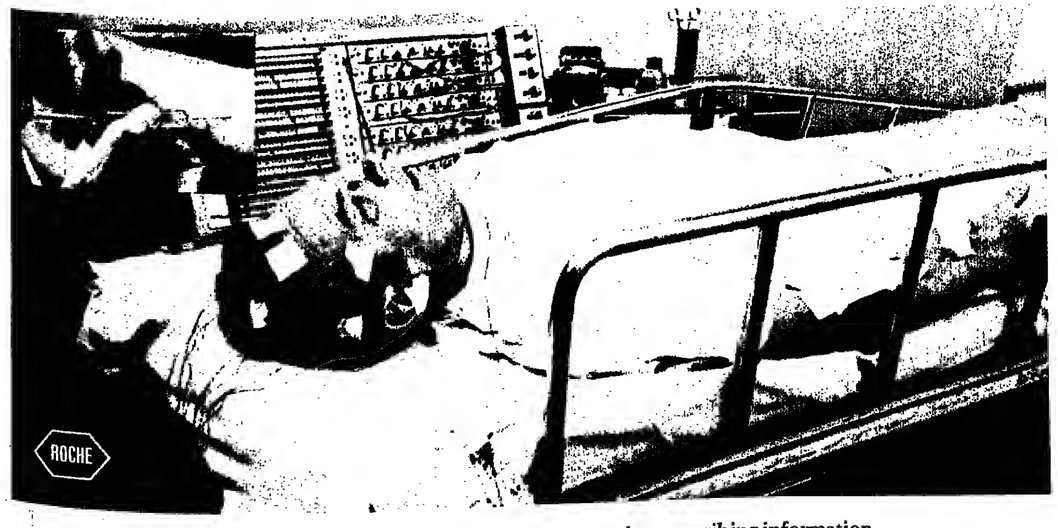
Five to ten minutes before elective cardioversion, the recommended dosage is 5 to 15 mg, injected slowly I.V. (5 mg/min).

The anticonvulsant effect of Valium® (diazepam)

adjunctively in certain convulsive disorders

Injectable Valium (diazepam) has usually been an effective adjunct in interrupting status epilepticus promptly, sometimes in a matter of seconds. It has helped provide control with the first injection, frequently with prolonged relief. Oral Valium may be used adjunctively in certain convulsive disorders such as petit mal or myoclonic seizures, although it has not proved useful as sole therapy.

In status epilepticus and severe recurrent convulsive seizures, 5 to 10 mg, injected slowly I.V.—5 mg (1 ml)/minute. Use I.M. route if slow I.V. injection is not feasible. Do not mix or dilute with other drugs, solutions or fluids. Repeat in 2 to 4 hours, if necessary. The dosage for Oral Valium used adjunctively is 2 to 10 mg, 3 or 4 times a day.



Please see the last page of this advertisement for complete prescribing information.

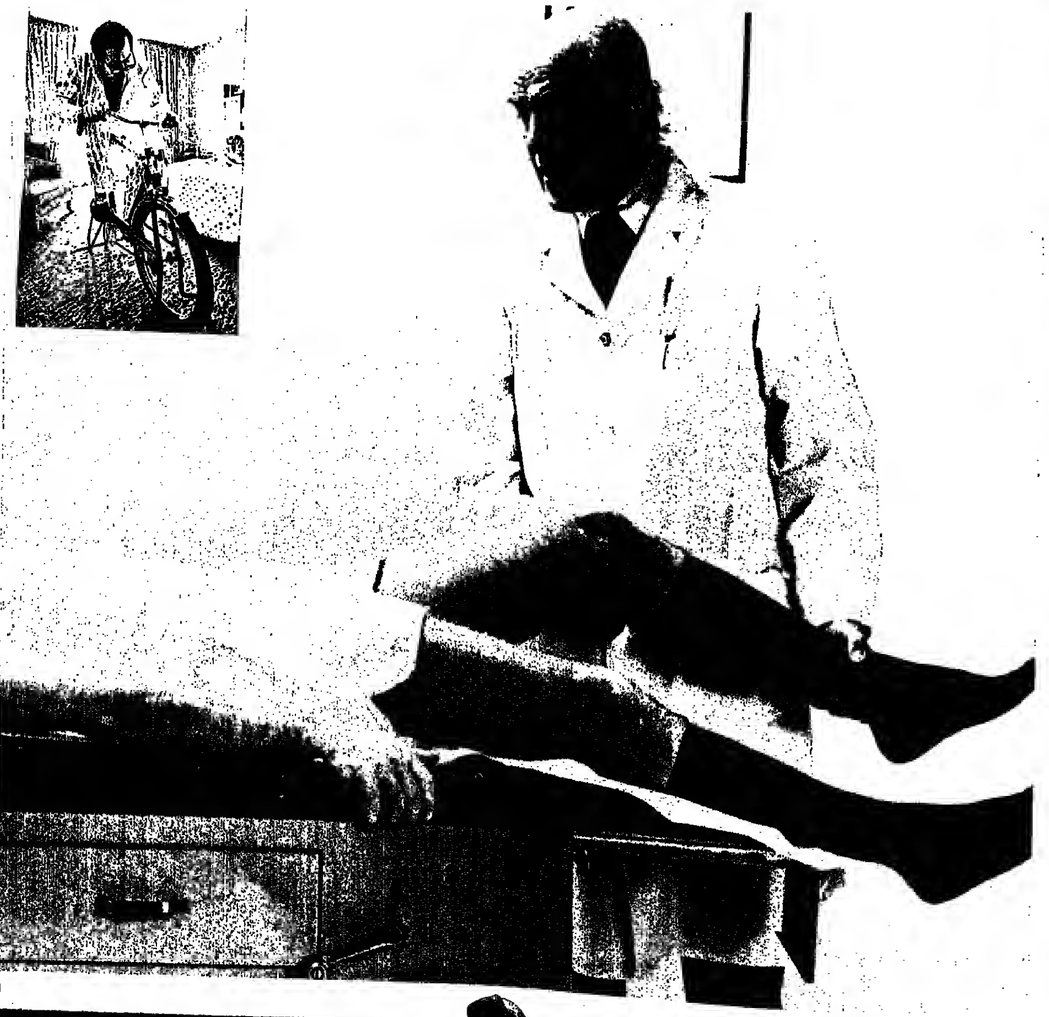
The skeletal muscle relaxant effect of Valium® (diazepam)

adjunctively in skeletal muscle spasm caused by local pathology

As part of the therapeutic regimen, Valium (diazepam) orally or parenterally, as appropriate, can help relieve skeletal muscle spasm due to reflex spasm caused by local pathology, such as inflammation of muscles or joints, or associated with muscle strains. It can help break the spasm/pain/spasm cycle and thus may increase mobility.

Usual oral dosage is 2 to 10 mg on a *t.i.d.* or *q.i.d.* schedule.

Usual injectable dosage is 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours, if necessary. In elderly or debilitated patients, it is recommended that oral dosage be limited to the smallest effective amount to preclude the development of ataxia or oversedation (2 to 2½ mg once or twice daily, initially, to be increased gradually as needed and tolerated).



For three different effects:
psychotherapeutic
anticonvulsant
skeletal muscle relaxant

Valium® (diazepam) ROCHE

adjunctively in spasticity associated with paraplegia

In upper motor neuron disorders causing paraplegia, the adjunctive use of Valium (diazepam) can help reduce skeletal muscle spasticity. Valium offers a wide margin of safety due to its relatively low toxicity. Isolated reports of neutropenia and jaundice make periodic blood counts and liver function tests advisable during long-term therapy.

Three convenient tablet strengths—2 mg, 5 mg, 10 mg—allow wide adjustments in dosage for the greatest efficacy in clinical response. And Injectable Valium may be used, where appropriate, in the usual dosage for muscle spasm.

adjunctively in spasticity due to cerebral palsy or athetosis

The skeletal muscle relaxant effect of Valium (diazepam) makes it a valuable adjunct in reducing spasticity. It may thus aid by reducing involuntary movements and improving voluntary performance and speech. This may result in more patient cooperation and confidence during therapy. Valium is generally well tolerated; drowsiness has been the biggest problem among responsive athetoid children. The possible side effect of ataxia may limit its usefulness in ataxic children.

Dosage should be individualized for maximum patient benefit. However, the usual recommendation is 2 to 10 mg *t.i.d.* or *q.i.d.* Where parenteral therapy is indicated, use 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours, if necessary. Oral Valium is contraindicated in children under 6 months. Injectable Valium is contraindicated in infants and its safety and efficacy in children under 12 have not been established.

parenterally in stiff-man syndrome or in tetanus

Injectable Valium (diazepam), used adjunctively, can reduce characteristic skeletal muscle spasm and resulting rigidity. Response is usually prompt and improvement sustained in the control of muscular rigidity and convulsive spasms. In general, Valium can thus help improve range of mobility. Periodic blood counts and liver function tests are advisable during long-term therapy. Only the parenteral form of Valium (diazepam) is indicated for tetanus. Usual I.M. or I.V. dosage recommendation is 5 to 10 mg; for tetanus, larger doses may be required. A repeat dose, if necessary, may be administered in 3 to 4 hours.

Please see the following page for complete prescribing information.

Antigen Barred as Colorectal Cancer Screen

Medical Tribune Report

BAL HARBOUR, FLA.—Carcinoembryonic antigen (CEA), though useful for diagnosis of colorectal cancer, lacks specificity for use in screening, a study by the National Cancer Institute of Canada and the American Cancer Society concludes.

Specimens were studied at four university centers in the United States, with the Montreal General Hospital laboratory serving as reference center. Of the 503 patients admitted to the study, 146 had cancer of the colon or rectum; 62 per cent of preoperative specimens from these patients were positive for CEA, as were 53 per cent of specimens from patients with other types of cancer and 29 per cent of patients with other diagnoses. Anthony B. Miller, M.B., of the Canadian institute, reported results at the American Cancer Society's second National Conference on Cancer of the Colon and Rectum here.

Dr. Paul Lo Gerfo, College of Physicians and Surgeons, Columbia University, reported on the prognostic value of high and low CEA levels in 158 patients with nonmetastatic colon carcinoma over 18 months of follow-up.

In general, he said, high preoperative levels of CEA were associated with poorer prognosis. Increased CEA values were found in 57 per cent of patients who died compared with only 32 per cent of patients who remained alive and well.

Dr. Norman Zamcheck, Harvard Medical School, confirmed both the positive correlation between poor prognosis and high preoperative CEA levels and the relative nonspecificity of CEA. Assays are positive in 45-60 per cent of early, resectable colorectal cancer patients and in 90 per cent of late or metastatic cases. When resection of the primary colonic malignancy is complete, previously elevated CEA levels usually drop, he noted.

Though CEA is not specific for cancers of the digestive tract—assays are also positive for nonendodermal cancers and for such nonneoplastic diseases as cirrhosis of the liver, alcoholic pancreatitis, and ulcerative colitis—the levels in benign disease are lower than in malignancies.

Dr. Zamcheck stressed that quantitative, not qualitative, differences in the amount of circulating CEA are useful clinically, that the assays cannot substitute for complete clinical and laboratory study, and that they are not useful for making a specific diagnosis of colon cancer in screening patients.

Disease Like Diabetes Affects Some Animals

Medical Tribune World Service

BRUSSELS—A wide range of animal species are affected by a syndrome closely resembling diabetes mellitus in man.

The list so far includes not only domestic animals but also a hippopotamus in Tokyo Zoo, two performing dolphins, and a fox found to be diabetic at the end of a hunt. Japanese workers have also identified a disorder similar to diabetes in two species of fish.

Of special importance to research workers are the syndromes associated with hyperglycemia in smaller animals, all of them rodents, Prof. A. B. Renold, of the University of Geneva Medical School, pointed out in his Claude Bernard lecture to the eighth Diabetes Congress here.

In some instances insulin secretion is decreased relatively early in the life of the predisposed animals, Dr. Renold said. This is true for certain sublines of the Chinese hamster, for New Zealand obese mice at some point during the evolution of their syndrome, and for the spiny mice, Acomys cahirinus, in which insulin secretion is decreased throughout life.

One Man...and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

A Noble Man

WITH THE DEATH of Gustaf VI Adolf, Sweden lost a unique king and the world its oldest ruling sovereign.

Oscar Fredrik Wilhelm Olaf Gustaf Adolf was a man who was as unpretentious as he was beloved, as accomplished a botanist as he was an archaeologist, as great a linguist as he was an art connoisseur, as outstanding a scholar as he had been an athlete. His simplicity was offset by his remarkable perspective and humor. His sense of discipline and proportion was unusual in a man of his birth but consistent with his accomplishments and his talents. Once, in Venice for an exhibition of archaic jades, he expressed deep interest in a very fine piece. Upon learning its price, he amiliugly remarked, "A beautiful piece of carving, but too expensive for the poor King of Sweden."

Gustaf VI Adolf was a man of the world in the truest sense. His was a multinational genetic inheritance. He was the great-great-grandson of Jean Baptista Bernadotte, one of Napoleon's generals, and son of a princess of the Grand Duchy of Baden in Germany. His first wife, Princess Margaret of Connought, was a granddaughter of Queen Victoria of England, and his second wife, Lady Louise Alexandra Marie Irene Mountbatten, sister of Earl Mountbatten of Burma, was a great-granddaughter of Queen Victoria.

It was in 1963 when I had first received an invitation from Gustaf VI Adolf to attend the opening of the new Museum of Far Eastern Antiquities in Stockholm. My mother's terminal illness had necessitated a cancellation of that visit. Later, in Greece, when I was attending a medical congress, I saw him by chance in Athens, where he was attending the wedding of the Danish princess to the King of Greece. Some months ago I missed him after having made arrangements with Bo Gyllensvärd, Keeper of his collection, to meet in London with Gustaf VI Adolf and his personal physician, Gunnar Biorck.

Visited Him a Year Ago

About a year ago I visited the King's private apartment in the Royal Palace in Stockholm and shared that visit with you in this column. His apartment was one in which he had lived as crown prince. He never moved after the simple ceremony which marked his "taking the throne." His personal unpretentiousness but deep and varied interests were reflected in each room. Despite the dimensions of the palace, one felt quickly "at home" in a dwelling which reflected the multiple interests of a scholar and archaeologist, a collector, and, above all, a world citizen. Gustaf VI Adolf was *nu courant* with modern archaeology and particularly interested in the fusion of the physical sciences with art history. He was fascinated by the x-rays of his bronzes, the use of carbon^{14} in the dating of organic materials, and the recently developed datiog technique of thermoluminescence for ceramics. While he loved beautiful pots, lacquer, and born carvings, he was particularly devoted to Chinese ritual bronzes and early jades.

Gustaf VI Adolf held honorary degrees from Princetoo, Yale, Harvard, the University of Pennsylvania, Clark University, Lafayette College, and the University of Chicago and was probably one of the few men of royal lineage who had actually earned them. He eojoyed travel and spent much time in England. For many years he was unable, "for reasons of state," to visit the United States, which he would have particularly enjoyed because of his interest in the great American collectioos of Chinese antiquities. Due to his age, his travel was restricted in terms of distaoce and climate. Supporters of the Swedish monarchy who were deeply concerned with its continuance believed the continuing reign of Gustaf VI Adolf vital for the transition to his grandson, now Carl XVI Gustaf, who at 27 is the youngest ruling monarch in Europe. In lieu of his personal visits, the King's collection of Chinese art and archeology, representing 4,000 years of history, came to the United States and was exhibited at the National Gallery in Washington and Asia House in New York.

Interests Were Not Passive

Just as Gustaf VI Adolf was active in early life in athletics—an expert marksman, a gifted horseman, a tennis player, and a skier—his scholarly interests were not a passive but a constant and growing personal participation. His studies in art history were supplemented by his work in field archaeology. While his greatest concentration had been on Etruscan digs, he previously had done field work in Sweden, Greece, Egypt, and China.

Gustaf VI Adolf's botanical work won him what was, for a monarch, a rare honor —membership in Britain's Royal Academy. His sensitivity to his role as a sovereign led him to forgo his rightful place among those scholars who did so much for our classification of Chinese bronzes and jades. He worked as collaborator but did not appear as coauthor.

I will never forget a fascinating incident which Bo Gyllensvärd, the King's curator, described to me. We had been discussing the King's interest in Chinese lacquer and the outstanding collection of a Chinese specialist in the field. This particular Chinese collector is renowned not only for his dedication, interest, and knowledge of this field but also for a passionate bluntness not usually associated with the so-called enigmatic and polite ways of the East. At one point in the discussion between the Swedish King and the Chinese connoisseur, the collector grasped Gustaf VI Adolf by the lapels of his jacket and with the greatest intensity exclaimed, "King, this is absolutely correct!" After he left, His Majesty turned to his curator and with his typically engaging smile said, "That was an unusual experience."

All who love art and its history, all who have admired the fruitful and stimulating contributions of Swedish science and the Nobel awards, all who appreciate scholarship and connoisseurship, and all who respect greatness with humility will miss that truly noble man, Gustaf VI Adolf.

EPIGRAMS

I have often thought that the best way to define a man's character would be to seek out the particular mental or moral attitude in which, when it came upon him, he felt himself most deeply and intensely alive. At such moments there is a voice inside which speaks and says: "This is the real me!"

William James, M.D. (1842-1910)
writing to his wife
The Letters of William James

The Somatic Protest in duodenal ulcer

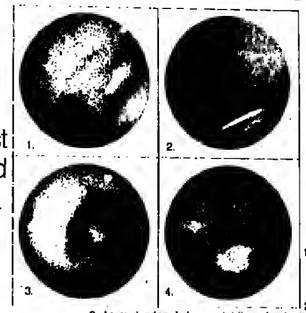
Excessive anxiety can exacerbate symptoms

Excessive emotional tension and anxiety are believed to cause adverse changes in the physiology of the stomach or the duodenum and thereby often contribute to the pathogenesis and aggravation of peptic ulcers. Although the exact causative mechanism remains to be elucidated, gastric hypersecretion and intestinal hypermotility are, in many patients, end-organ manifestations, and these processes usually give rise to typical symptoms of duodenal ulcer.

Whenever immoderate, harmful anxiety is prominent in the clinical profile, consider—

in addition to primary therapy—the adjunctive use of Librium to effect reduction of anxiety-linked gastrointestinal complaints or symptoms. Librium is used concomitantly with certain specific medications of other classes of drugs, *e.g.*, anticholinergics and antacids.

Librium has an excellent record of *effectiveness with safety*. After more than 13 years of wide clinical use, Librium continues to demonstrate its highly favorable therapeutic index. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated. When excessive anxiety has been reduced to appropriate, tolerable levels, therapy with Librium should be discontinued.



1. Acute duodenal ulcer and duodenitis associated with a constriction deformity of the distal duodenal bulb
2. Acute duodenitis
3. Acute duodenal ulcer and diffuse duodenitis, seen through the pylorus
4. Acute duodenal ulcer and duodenitis, seen intraduodenally

For relief of moderate to severe anxiety in duodenal ulcer patients adjunctive

Librium® 10 mg (chlordiazepoxide HCl)

1 or 2 capsules t.i.d./q.i.d.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various diseases states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Librium® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

. . . brief summaries of editorials or guest editorials in current medical journals.

Who, Me?

"When the senior practitioners among us were just starting in, the medical societies had a rather rigid, dogmatic ban on anything that might be construed as advertising. If a physician's name appeared in the newspapers, even in the context of a social note, a public speech, or advertising for a lost dog, this publicity was assumed to be self-aggrandizement." However, the latest edition of the A.M.A.'s *Principles of Medical Ethics* simply omits any reference to advertising or self-aggrandizement.

"This is, perhaps, a belated but realistic acknowledgment of the situation today. If you have under your care a man or woman of considerable prominence, you may be besieged by reporters who will publish the name of the treating physician and there isn't anything you can do about it. Note that the 1955 [A.M.A.] canons of ethics specifically condemn comments about the institution as well as the individual practitioner. Today hospitals and medical centers often have public relations departments which strive to get the institution's name in the papers. The public has a right to know, has a deep interest in medicine and surgery, and wants to keep apprised of medical and surgical progress. . . . Perhaps some of us may offer a requiem on the disappearance of a quaintly old-fashioned ethical principle, but this is one of the facts of life of 1973." Editorial, *(J. Med. Soc. New Jersey 70:629, September, 1973.)*

A Time for Everything

"An architect friend of mine sees no reason why we should not adapt to a concrete jungle, and he includes aesthetic adaptation. He sees the purpose of our environment as primarily commercial, its use as the meeting of our simple physiological needs. His argument is that what we will not know or cannot perceive we shall not miss. . . . [But] should we deny ourselves the sight of beauty, because by so doing we will not know the value of our loss? But in any case for thousands of years there have been evoked in us certain responses to natural sights and sounds that were established and prevailed over a span of centuries that makes infinitesimal the period of time that has seen the existence of vast environments of brick and concrete. Who would not even now stop in their tracks at the sound of the nightingale, or feast replete on the sparkle of the sun on the fresh moving sea? To cast these aside is to ignore the legacy of a thousand ages. . . .

"In answer to the architect, I proclaim the environment does matter, although you cannot just surround an individual by what is appropriate and expect miracles. . . . From the urban boy we need moments of primitive contrast." Dr. M. D. Coulter, personal view. *(Brit. Med. J. 3:345, August 11, 1973.)*

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Vitamin C May Help Block Carcinogenesis

Medical Tribune Report

EAST LANSING, MICH.—Should we add vitamin C to such cured meats as hot dogs and bacon—containing the preservative sodium nitrite—as a possible way to block formation of a carcinogen?

Evidence in favor of this, now under consideration by Government investigators, emerged from studies on rats reported here at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, held at Michigan State University.

A research group from Hoffmann-La Roche, Inc., administered sodium nitrite plus aminopyrine (a tertiary amine) orally to rats. These substances react in the acidic environment of rat stomach to form nitroso derivatives that cause an acute hepatotoxicity and that may possess carcinogenic activity, according to Theodore Dashman, who described the experiments.

Peak serum levels of dimethylnitrosamine (DMNA) were seen 30 minutes following the dose of the nitrite-aminopyrine combination, Mr. Dashman said. But in contrast, animals that were given ascorbate at the same time showed almost no DMNA in serum 30 minutes later.

"The conclusion is that DMNA is formed from the reaction of aminopyrine and sodium nitrite in vivo and that ascorbate inhibits the formation of DMNA," he commented.

The report noted that only two amines, dimethylamine and aminopyrine, proved hepatotoxic when given with sodium nitrite. Ascorbate guarded against both.

Anticancer Notion Discounted

In an interview following the formal report, Jerome J. Kamm, Ph.D., who heads the research team, told MEDICAL TRIBUNE that he discounts the notion of vitamin C as an "anticancer" substance.

"Ascorbate is not preventing cancer," Dr. Kamm said. "Ascorbate is preventing a chemical reaction."

"What we are looking at here is an acute hepatotoxicity," he continued. "It's very possible that very small amounts of the nitrosamine were indeed formed, which we couldn't measure, and nobody knows how much of the nitrosamine is required to produce a cancer. So whether or not this [use of ascorbate] will prevent cancer formation is a completely different story."

Dr. Kamm also emphasized the investigators' finding that vitamin C—to exert its protective effect—must be in the stomach at the same time as the nitrite-aminopyrine combination.

He pointed out that if the same protection against hepatotoxicity is demonstrated in man, it would not help "to take vitamin C tablets in the morning and then proceed in the afternoon to eat foods containing amines and nitrite."

Asked if he believes that the vitamin should be added to foods that contain naturally occurring amines along with nitrite used as a preservative, Dr. Kamm said the possibility is being actively studied by both food processors and the Government.

Other members of the investigative group were Allan H. Conney, Ph.D., and John J. Burns, Ph.D., who is vice-president and director of research.

Osaka's VD Sources

Medical Tribune World Service

OSAKA, JAPAN—The main source of venereal infection for men treated at medical centers in Osaka prefecture is bar hostesses and geishas, and nearly half the women patients questioned contracted the disease from their husbands.

Medicine at Stamps

Pedanius Dioscorides

Pedanius Dioscorides (ca. A.D. 40-90) was born a Greek and educated in the Greek medical centers. Later, serving in Nero's armies, he became the most famous army surgeon in the Roman Empire. His *Materia Medica*, written A.D. 73-77, was the first comprehensive and scientific study of plants, their source, preparation, and use for specific illnesses. It remained the authoritative work on the subject for more than 15 centories.

The Yemen Arab Republic issued the stamp in 1967 in an art series reproducing Asian paintings.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Women With Severe Diabetes Advised to Avoid Pregnancy

Medical Tribune World Service

BRUSSELS—Women with severe diabetes should be strongly advised by their physicians to avoid pregnancy, particularly when vascular complications exist, Dr. Paul Beck, Associate Professor of Medicine at the University of Colorado, declared here.

Sterilization is the safest and surest method in such a situation, he said.

Dr. Beck, speaking at the eighth Congress of the International Diabetes Federation, said that it is important to avoid the difficulties created by pregnancy when possible, and perhaps also to avoid adding to the genetic pool of diabetics.

It is recognized that oral contraceptives can produce a number of metabolic changes in normal women, he said.

"Their effect on carbohydrate and lipid metabolism," he continued, "appears to be related to the patient's age and predisposition to metabolic disease and to the amounts and proportions of estrogen, nortestosterone, and progesterone in the pill.

"Changes in each of the metabolic factors—glucose, insulin, cholesterol, and triglyceride metabolism—are usually small, and blood pressure alterations are infrequent in the nondiabetic population. However, each factor has been related to an acceleration of atherosclerosis in both normal and diabetic women. Consequently, we must take a hard look at the possible results of prolonged use of these drugs on the cardiovascular health of the patient."

Women with borderline pancreatic insulin reserve appear more likely to develop abnormal glucose tolerance than normal women when given oral contraceptives, Dr. Beck said, although deterioration of glucose homeostasis has not been found too often in insulin-requiring diabetics who are taking the pill. Yet the lack of change in the diabetic insulin requirements must be balanced against potential changes in lipid concentrations.

Deterioration of glucose tolerance is greatest during treatment with mestranol plus a nortestostarone derivative in women with ovart hyperglycemio not using insulin, as well as in women with latent hyperglycemia provoked by pregnancy or glucocorticoids, Dr. Beck said.

The following briefs were excerpted from reports presented at a course for physicians in private practice on the treatment of children with minimal brain dysfunction. The two-day course, held in New Orleans, was jointly sponsored by the Division of Continuing Education, Louisiana State University School of Medicine, Division of Child and Adolescent Psychiatry, University of Arkansas Medical Center, and CIBA Pharmaceutical Company, as part of its Medical Horizons Postgraduate Education Series.

Child Development

"No concern should have higher national priority than that of providing the fullest opportunity for physical and intellectual development for every child," Dr. John E. Peters said.

"Yet for the MBD child the availability of special resources required for the accomplishment of this goal is extremely limited."

Dr. Peters, Professor of Psychiatry at the University of Arkansas, directed the MBD course.

Parents' Role in MBD

Various behavioral symptoms of minimal brain dysfunction (MBD) are present in the first year of life and may elicit parental response that exacerbate the situation, according to Dr. Nancy R. Haslett, who is Assistant Professor of Psychiatry and Neurology at Louisiana State University.

"Later behavioral problems probably stem from disturbed parent-child relationships as much as from neurologic dysfunction," she said.

"Intervention programs should attempt to alter the patterns of destructive parent-child interactions. For example, babies who are exquisitely sensitive to changes in routine or to sudden noises should be protected. Mothers could be counseled on methods of dealing with their hyperirritable babies who sleep erratically and feed poorly."

Agent Given Test In Colds; Result Is Unencouraging

Medical Tribune Report

WASHINGTON—The antiviral chemical 3,4-dihydro-1-isoquinolineacetamide hydrochloride (DIQA) appears to have only a "very weak" antirhinoviral effect in human beings, according to University of Maryland investigators. Doses of DIQA failed to prevent the development of colds in healthy male volunteers following viral challenge, Dr. Andrew R. Schwartz told the Interscience Conference on Antimicrobial Agents and Chemotherapy here.

The 21 subjects had absent or minimal serum neutralizing antibody to rhinovirus. Ten received DIQA and 11 got placebos. On the first day of the seven-day study, volunteers received either a 500-mg. capsule of DIQA or a placebo before dinner and at bedtime. Viral challenge was given intranasally on the second day, followed two hours later by the medication, which was repeated before each meal and at bedtime for the next 5 days.

Over-all symptoms were "somewhat greater" among the placebo recipients, but this was not statistically significant. Those symptoms appearing both more severe and more frequently among the placebo group included rhinorrhea, nasal stuffiness, headache, coughing, and sneezing. Rises in serum neutralizing antibody titers were fore frequently detected among the patients receiving DIQA.

Coauthors were Drs. Yasushi Togo and Richard B. Hornick.

Two ways to treat essential hypertension and why...

Esimil®

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

INDICATIONS
Esimil
Hypertension. (See box warning.)

Ser-Ap-Es
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows: Effective: Hypertension. (See box warning.)

WARNING
This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

CONTRAINDICATIONS
Esimil
Guanethidine: Known or suspected pheochromocytoma; hypersensitivity; frank congestive heart failure not due to hypertension; use of MAO inhibitors.
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.
Ser-Ap-Es
Reserpine: Known hypersensitivity; mental depression (especially with suicidal tendencies); active peptic ulcer; ulcerative colitis; electroconvulsive therapy.
Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.
Hydrochlorothiazide: See hydrochlorothiazide section above.

WARNINGS
Antihypertensives are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with all drugs and their combinations before prescribing, and patients should be warned not to deviate from instructions.
Esimil
Guanethidine

Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. To help prevent fainting, warn patients to sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during the initial period of dosage adjustment and with postural changes. The potential occurrence of these symptoms may require alteration of previous daily activity. Caution patients to avoid sudden or prolonged standing or exercise while taking the drug.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.
If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage and have oxygen, atropine, vasopressors, and IV solutions ready for immediate use to treat vascular collapse. Vasopressors should be used with extreme caution in patients on guanethidine because of the possibility of augmented response and the greater propensity for cardiac arrhythmias.
Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma, since their condition may be aggravated.
Hydrochlorothiazide
Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
Thiazides may be additive or potentiative of the action of other antihypertensive drugs.
Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.
Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.
The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.
Ser-Ap-Es
Reserpine: Use with extreme caution in patients with a history of mental depression. Discontinue at first sign of despondency, early morning insomnia, loss of appetite, impotence, or self-depreciation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide. MAO inhibitors should be avoided or used with extreme caution.
Hydralazine: Chronic administration of doses over 400 mg daily may produce an arthritis-like syndrome simulating acute systemic lupus erythematosus. This may also occur at lower doses. Long-term treatment with steroids may be necessary and residua have been detected many years later. CSC's, L.E. cell preparations, and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine or if the patient develops any unexplained signs or symptoms.
Use MAO inhibitors with caution.
Hydrochlorothiazide: See hydrochlorothiazide section above.
Usage in Pregnancy
Esimil
Guanethidine: The safety of guanethidine for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.
Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.
Nursing Mothers
Thiazides cross the placental barrier and appear in cord blood and breast milk.
Ser-Ap-Es
Reserpine: The safety of reserpine for use during pregnancy or lactation has not been established; therefore, the drug should be used in pregnant women, in the judgment of the physician, only if essential to the welfare of the patient. Increased respiratory tract secretions, nasal congestion, cyanosis, and anorexia may occur in neonates and breast-fed infants of reserpine-treated mothers since reserpine crosses the placental barrier and appears in maternal breast milk.
Hydralazine: The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.
Hydrochlorothiazide: See hydrochlorothiazide section above.

PRECAUTIONS
Esimil
Guanethidine: The effects of guanethidine are cumulative over long periods; initial dose should be small and increased gradually in small increments. Use very cautiously in hyperthyroidism or rising BUN levels; coronary disease with insufficiency or recent myocardial infarction; cerebral vascular disease, especially with encephalopathy. Do not give guanethidine to patients with severe cardiac failure except with extreme caution.
In incipient cardiac decompensation weight gain or edema may be averted by the administration of a thiazide. Remember that both digitalis and guanethidine slow the heart rate.
Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.
Amphetamine-like compounds, stimulants (eg, ephedrine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine) and other psychopharmacologic agents (eg, phenothiazines and related compounds), and oral contraceptives may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting guanethidine.
Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia).
Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medications such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.
Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.
Interference with adequate oral intake of electrolytes will also contribute to hypokalemia.
Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.
Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.
Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.
Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.
Ser-Ap-Es
Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or gallstones (biliary colic may be precipitated). Exercise caution when treating hypertensives with renal insufficiency. Use cautiously with digitalis and quinidine.
Intraoperative hypotension has occurred in hypertensive patients receiving rauwolfia preparations, but withdrawal of reserpine does not assure that circulatory instability will not occur in such patients.
Hydrazine: Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.
Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to this regimen if symptoms develop.
Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.
Hydrochlorothiazide: See hydrochlorothiazide section above.

ADVERSE REACTIONS
Esimil
Guanethidine: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. *Frequent reactions due to unopposed parasympathetic activity*—bradycardia, increase in bowel movements, diarrhea (may be severe and necessitate discontinuance of the drug).
Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. *Other less common reactions*—dyspnea, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (anginal, chest paresthesias, nasal congestion, weight gain, and asthma in susceptible individuals. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia, and leukopenia have been reported.
Hydrochlorothiazide: Gastrointestinal—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo, paresthesias, headache, xanthopsia. *Dermatologic-hypersensitivity*—purpura, photosensitivity, rash, urticaria, necrotizing angiitis, Stevens-Johnson syndrome, and other hypersensitivity reactions.
Hematologic—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. *Cardiovascular*—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. *Other*—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.
Ser-Ap-Es
Reserpine: Gastrointestinal—hypersecretion; nausea; vomiting; anorexia; diarrhea. *Cardiovascular*—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. *Central Nervous System*—drowsiness; depression; nervousness; paradoxical anxiety; nightmares; rare parkinsonian syndrome and other extrapyramidal tract symptoms; CNS sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, and optic atrophy). *Miscellaneous*—frequently nasal congestion; pruritus; rash; dryness of mouth; dizziness; headache; dyspnea; syncope; epistaxis; purpura and other hematological reactions; impotence or decreased libido; dysuria; muscular aches; conjunctival injection; weight gain; breast engorgement; pseudoacteion; gynecomastia; rarely water retention with edema in hypertensive patients.
Hydralazine Common—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent*—nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and one instance of hypoglycemic paradoxical pressor response.
Hydrochlorothiazide: See hydrochlorothiazide section above.

DOSAGE
Esimil
As determined by individual titration (see box warning).
Note: 10 mg guanethidine monosulfate present in Esimil is equivalent to 8.4 mg guanethidine sulfate USP.
Before starting therapy, consult complete product literature.
Ser-Ap-Es
As determined by individual titration (see box warning).
Usual dosage is 1 or 2 tablets t.i.d. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.

HOW SUPPLIED
Esimil
Tablets (white, scored), each containing 10 mg guanethidine monosulfate and 25 mg hydrochlorothiazide: bottles of 100.
Ser-Ap-Es
Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 100 and 1000.
Consult complete literature of both products before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

CIBA

why Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

because only Ser-Ap-Es adds Apresoline® (hydralazine) to rauwolfia-thiazide—for direct action on arterioles

Only Ser-Ap-Es combines *Apresoline*—for direct peripheral vasodilation—with rauwolfia-thiazide.

Allows for smaller doses of each component.

If there is slight renal impairment, *Apresoline* helps maintain or increase renal blood flow.

If the patient is stress-reactive, the *reserpine* component should have a calming effect.

Hydrochlorothiazide provides both antihypertensive and saluretic actions.

Ser-Ap-Es, in a single tablet, has all the medication many hypertensives will need.

Use cautiously in patients with advanced renal damage or cerebrovascular accident. Discontinue at first sign of mental depression.

why Esimil®

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

because Esimil offers the control-with-convenience so many hypertensives need

Esimil contains guanethidine, perhaps the most effective antihypertensive drug available.

By effectively lowering blood pressure, it takes the pressure off target organs.

If the patient is free of organ damage, Esimil may help keep her that way. Tolerance with Esimil is infrequently a problem.

The convenience of Esimil is also worth noting: its simple once-a-day dosage is easy on the patient, certainly easy to remember.

Postural hypotension may occur with the use of Esimil, particularly while the drug is being introduced. Like all antihypertensives, Esimil should be given with caution in the presence of severe coronary insufficiency or recent myocardial infarction. Esimil is not indicated for initial therapy of hypertension.

early, effective control of hypertension can save lives

Institutionalized 98 Years—Reason Unknown

UPI Photo

At the age of four, 98 years ago—yes, that is correct, 98 years ago—Martha Nelson was admitted to the Columbus State Institute for the Feeble Minded in Ohio. She was later transferred to the Orient State Institute where her records were destroyed by fire in 1883, so no one now knows why the 102-year-old woman was originally admitted. Dr. A. Z. Soforenko, superintendent of Orient, calls her quite coherent for her age. Martha has not been visited by anyone for about 80 years.

Nerve Regeneration Speeded By Electromagnetic Energy

Medical Tribune Report

NEW YORK—The rate of regeneration of peripheral nerves in rats is significantly accelerated by exposure to pulsed electromagnetic energy, Dr. D. H. Wilson, consultant surgeon at the General Infirmary, Leeds, England, reported here.

In experiments described at the Conference on Electrically Mediated Growth Mechanisms in Living Systems, the median-ulnar nerve in the left forelimb of a series of pairs of rats was divided and sutured. Subsequently, one rat from each pair was treated daily by exposure to pulsed electromagnetic energy.

Healing time for surgical incisions was four days in the treated rats as compared with seven days in the control animals. Treated rats began to use their left forelimb after 10 days, untreated rats not until 21 days.

Nerve conduction studies at 12 days showed a modified response in the treated nerves but none in the untreated. At 30 days a biphasic action potential was demonstrated in the treated animals, and at 45 days their nerve conduction tracings were indistinguishable from normal. Nerve conduction did not begin to return in the untreated nerves before 60 days.

Dissection of nerves for histologic studies revealed considerably less scarring and fibrosis around the nerve suture sites in the treated rats, suggesting that "there was also less fibrous tissue formed between the two halves of the nerves, thus permitting the more rapid recovery." Comparison of histologic preparations of nerves showed that treated nerves had recovered more fully at 30 days than untreated nerves had at 60 days.

Nerves Cleanly Divided

Regarding clinical applicability, Dr. Wilson cautioned that in his experiment the nerves were cleanly divided without complicating damage to surrounding tissues and were anastomosed within minutes. Furthermore, therapy was begun only two hours postoperatively, and comparable dosage for human beings would be impractically high. However, the experimental dosage was "quite empirical," and therefore "further experimentation may show that the same results can be obtained with a smaller dosage."

The nerve regeneration experiments grew out of a previous study comparing the effectiveness of conventional shortwave diathermy and pulsed electromagnetic energy in treatment of ankle sprains in human subjects. Results showed that in pairs of patients matched for sex, age, weight, and degree of trauma, short-wave diathermy produced a 44 per cent recession of symptoms in three days with a total energy transfer of 22 watt-hours, whereas only 15 watt-hours of pulsed electromagnetic energy therapy produced an 82 per cent recession of symptoms in the same period. "This finding throws very considerable doubt on the theory that using pulsed electromagnetic energy as a means of therapy is merely another method of generating heat in the tissues."

Domestic Meetings

Nov. 1 ....American Pancreatic Study Group, *Chicago*
Nov. 1-3 .....Association for Academic Surgery, *Rochester, N.Y.*
Nov. 1-3 .....Central Society for Clinical Research, *Chicago*
Nov. 1-3 .....Florida Industrial Health Conference and Southeastern Industrial Health Conference, *Tampa*
Nov. 1-3 .....Southern Thoracic Surgical Association, *Louisville, Ky.*
Nov. 1-3 .....West Coast Allergy Society, *Honolulu*
Nov. 1-4 .....Pennsylvania Medical Society, *Harrisburg*
Nov. 2-4 .....Association of Clinical Scientists, *Washington, D.C.*
Nov. 2-4 .....Regional Laryngectomy Conference, *Framingham, Mass.*
Nov. 3 ....Conference of State and Provincial Health Authorities of North America, *San Francisco*
Nov. 3-7 .....American Urological Association, *Dorado Beach, P.R.*
Nov. 4 ....Association for the Advancement of Psychotherapy, *New York*
Nov. 4-6 .....American College of Obstetricians and Gynecologists, *Honolulu*
Nov. 4-6 .....American College of Preventive Medicine, *San Francisco*
Nov. 4-8 .....Association of American Medical Colleges, *Washington, D.C.*
Nov. 4-9 .....International and Civil Affairs Health Society, *San Francisco*
Nov. 5-7 .....Conference and Workshop on Embryonic and Fetal Antigen in Cancer, *Knoxville, Tenn.*
Nov. 5-7 .....International Health Society of the United States, *San Francisco*
Nov. 5-7 .....Society of Military Orthopaedic Surgeons, *El Paso, Tex.*
Nov. 5-9 .....Gerontology Society, *Miami Beach, Fla.*
Nov. 6-10 ....American Society of Tropical Medicine and Hygiene, *Houston, Tex.*
Nov. 7-9 .....American Cancer Society, *New York*
Nov. 7-10 ....American Medical Women's Association, *Palm Beach, Fla.*
Nov. 7-10 ....American Society of Cytology, *Salt Lake City*
Nov. 7-10 ....Puerto Rico Medical Association, *Santurce, P.R.*
Nov. 8-10 ....American Social Health Association, *New York*
Nov. 8-15 ....American Association for Cancer Education, *Honolulu*
Nov. 8-13 ....American Heart Association, *San Francisco*

Gardening Provides Enjoyable Exercise For the Handicapped

Over the years, gardening hes emerged as an increasingly popular aid in the rehabilitetion of the mentally and/or physicelly handicapped person. In November, professionals in the fiald will meet for the first time to form the National Council for Therapy and Rebebilitation Through Horticulture. Howard Brooks and Cherics Oppenheim, of New York University's Institute of Rehabilitation Medicine's greenhousc (shown here), have recently published a monograph on the subject, outlining many of their programs end techniques.

Metal spoons can be bent to help overcome physical deficiesciee and problems, and other simple tools can also be adapted easily.

Medical Tribune Photos—Luigi Pellarini

The work in the greenhouse offers not only exercise but also the experience of enjoying the warmth and beauty of flowers and plants. The experience raises the spirits of the patients and helps them to adjust to their handicaps.

Mr. Brooks (right) uses horticulture as one aspect of the patient's total program. Activities are based on goals established for the patient by his occupational or physical therapist.

Jamaica Study Finds No Harm In Chronic Use of Marijuana

Continued from page 1

and the results of in-hospital laboratory work, was submitted to HEW's National Institute of Mental Health in March, 1972, with no attendant publicity in this country.

In the clinical phase of the project, 30 confirmed smokers, in whom duration of regular use of marijuana ranged from seven to 37 years (mean of 17.5) were matched with 30 controls who either had never smoked or had never been regular smokers and had long ceased.

During a six-day period of abstinence from cannabis—while in University Hospital, Kingston, Jamaica—all 60 were assessed by detailed medical history and examination, heart and lung radiography, electrocardiography, respiratory function tests, blood chemistry, liver and renal function, hematologic studies and treponemal serology, and chromosomal studies. In addition, blood and urine samples were analyzed for peripheral thyroid hormone levels and steroid excretion.

None Had Used Hard Drugs

None of the 60 had ever used heroin, morphine, LSD, emphetamines, berbiturates, or jimson weed. Of the 30 confirmed smokers, 27 also used tobacco. Of the 30 controls, 19 were tobacco smokers. Eight controls had had slight experience with marijuana.

The number of cigarettes (spliffs) that had been consumed per day at the time of the study ranged from one to 24, with an average of seven. Light use was defined as one to four spliffs a day, moderate use as four to seven, and heavy use as eight or more a day. Smokers who used the pipe consumed from one to 25 pipefuls per week, with an average weekly consumption of 14. Marijuana samples submitted for analysis by the smokers had a mean Δ-9 THC content of 2.96 per cent.

Possession or use of marijuana being illegal, it had been agreed that no studies of acute affects could be undertaken in University Hospital. Only one smoker is known to have breached the agreement —in a fit of dedication to science: "Hear me why I smoke it. Although you told me not to, I feel if a man is tested for a week and he doesn't smoke, it makes no sense. When a man tests me, I want him to find evidence that the smoke comes off me, and if it's effective it will show up. But if I stop smoking when I leave home to go to the hospital, there's nothing left."

Blood pressures in both smokers and controls were within normal limits. Roentgenograms of the heart and lungs were normal in both groups, except for some scarring of the lungs in one of the controls. Smokers and controls were matched in height and in age, but the smokers were an average of seven pounds lighter, suggesting the possibility that habitual smoking causes some suppression of appetite.

No Abnormal Configurations

Abnormalities found in chromosome studies of peripheral blood cultures were slightly more frequent in the nonsmoker controls. Chromatid breaks and gaps were seen in 2.36 per cent of cells of marijuana smokers and in 2.90 per cent of cells of controls—not statistically significant. No abnormal configurations, exchanges, or dicentrics were seen.

"It appears that chronic cannabis use has no significant effect on the mitotic chromosomes of human peripheral blood lymphocytes in the Jamaican man. The incidence of mild chromatid breakage was no higher than that found in random Jamaican subjects."

There were minor ECG abnormalities in 30 per cent of both groups, perhaps indicating the prevalence of a cardiomyopathy that has been recognized in Jamaica, possibly attributable to an obliterative disease of the small coronary vessels, often associated with heavy tobacco consumption.

Hematologic studies revealed eosinophilia in 11 subjects, seven nonsmokers and four smokers—not statistically significant. No significant differences were found in other hematologic tests, with the exception of hemoglobin and monocyte count values. There were twice as many nonsmokers as smokers in the low-Hb (10-14 Gm./100 ml.) range. There were six smokers in the high (17-20 Gm./100 ml.) range; only one nonsmoker fell into this category. Twice as many smokers as nonsmokers had low (0-1 per cent) monocyte values; twice as many nonsmokers as smokers fell into the high (5-9 per cent) category.

Elevation of the liver enzymes, serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase, was found in seven subjects—three nonsmokers and four smokers—but did not indicate significant liver damage.

Several interesting trends were noted in respiratory function, indicating an association between frequency and duration of *smoking per se* (tobacco cigarettes, marijuana) with respiratory function and differences in blood chemistry. Chronic, heavy smokers (more than 20 tobacco cigarettes per day, plus chronic marijuana smoking) are at greater risk of functional hypoxia. No other statistically significant differences were established.

Arterial blood determinations of oxygen, carbon dioxide, pH, bicarbonate, and pulse rate, at rest and immediately after exercise, were made. The only statistically significant difference between smokers and controls on these measurements was that bicarbonate after exercise was found to be lower among smokers.

The excretion of a number of urinary steroids in the chronic smokers and matched controls was studied for indications of marked changes in adrenal cortical function in the smokers. Smokers and controls were compared for urinary metabolites of cortisol. No differences were found between the two groups, either by t-test or by nonparametric statistical tests. The results indicated no significant reduction in cortisol secretion in the group of chronic cannabis users, compared with the nonusers.

Thyroxine Content Determined

Total thyroxine and free thyroxine content were determined. The groups did not differ from one another.

Comparative examinations of the 60 men were conducted by two members of the Department of Psychiatry, University of the West Indies, to whom they were randomly assigned.

The objectives were to seek evidence of psychoses, of abnormalities of mood, thought, behavior, or perception, that might be attributed to marijuana. Eysenck Personality Inventory (short form) appraisals revealed no appreciable differences.

(The ward staff, unaware of which subjects were smokers, observed that those who were in fact smokers were more affable and more popular. Men of the nonsmoking group were more often thought to be neurotic, and were more often impatient with ward routines and discipline.)

No significant abnormalities emerged from mental status examinations. Only one subject, a nonsmoker, showed up as significantly depressed on the Hamilton Rating Scale. No score on either the Schizophrenic Rating Scale or the Wing Rating Scale was indicative of any disorder.

In view of the frequent reports that the use of cannabis leads to a ne'er-do-well "amotivational syndrome," particular attention was given to work records of the subjects. No significant differences were found between smokers and nonsmokers.

Electroencephalograms were obtained for all 60 subjects. No significant difference appeared between the two groups in definite abnormalities or equivocal cases. Further, most of the findings considered definitely abnormal or equivocal were focal in nature, unlikely to have been caused by any medication or drug effect.

Psychologic appraisals were done to see

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Jamaica Study Finds No Harm In Chronic Use of Marijuana

Continued from page 34

whether there were any nonacute, lingering, or irreversible neuropsychologic effects in chronic smokers during the hospital period, when they abstained long enough to be physiologically free of the active chemical constituents of cannabis.

(It is known that THC has a two-phase biologic half life in which the rapid phase lasts about 30 minutes and the slow phase 56 hours. By the time the men were tested, there could have been very little, if any, THC in their bodies.)

The tests yielded no consistent differences between smokers and nonsmokers, the data clearly indicating that long-term use by these men did not produce demonstrable intellectual or ability deficits when they were without the drug for three days. There was no evidence to suggest schizophrenic effects or brain damage.

In associated physiologic tests carried out in the field, independently of the hospital clinical studies, the work performance of farmers before, during, and after smoking of marijuana was closely observed by microanalysis of movements.

Total hoeing or soil-turning space covered, or work accomplished in number of plants reaped, was usually reduced per unit of time after smoking. The number of body movements per minute was often greater after smoking, but more movements were required to complete a given task.

Farmers believed that their work was more intense after smoking—that they were doing a better weeding job, for example—but "the extra movements per time and space unit may be related to cumulative inaccuracies, resulting in the need for repetition."

Psychologic tests yielded no consistent differences between smokers and nonsmokers, the authors reported, "the data clearly indicating that long-term [cannabis] use by these [subjects] did not produce demonstrable intellectual or ability deficits. There was no evidence to suggest schizophrenic effects or brain damage."

Case history data taken from both groups support a popular contention among Jamaican marijuana users that smokers are less frequently engaged in criminal activity than nonsmokers.

Hallucinations Not Reported

Questionnaires also revealed that hallucinations are not associated with smoking. Only a few smokers reported having bad visions of little male or female dancers, and then only under the influence of their first smoke—visions so stereotyped as to suggest that they were seen only because mythology says they are to be expected.

The director of the project for HEW was Vera Rubin, Ph.D., director of the Research Institute for the Study of Man. Lambros Comitas, Ph.D., Professor at Anthropology and Education, Teachers College, Columbia University, was co-director of this project.

The psychiatric testing was directed by Michael H. Beaubrun (M.B. Edin., FRCPsych., FACPsych., DFAPA), Professor of Psychiatry and head of the department, University of the West Indies. The nonpsychiatric clinical testing was directed by Eric K. Cruickshank, M.D., FRCP, Professor and Head of Medicine, University of the West Indies.

Vitamin E Held Unsuccessful In Easing of Angina Pectoris

Continued from page 1

An additional part of the trial also demonstrated, they said, that discontinuance (on a double-blind basis) of previously prescribed vitamin E therapy did not result in a statistically significant difference in anginal symptoms between placebo and vitamin-treated patients.

The first part of the trial was the examination of data on 36 patients, recruited for the study by their attending physicians. Criteria for enrollment included a reasonably stable angina, no major change in health status or in usual medication for at least three months, and dependability—patients had to take test capsules regularly and keep adequate records.

Half of this group took a daily dose of 3,200 I.U. of vitamin E for nine weeks, while the remaining 18 took an indistinguishable placebo. The amount of vitamin E, as alpha-tocopherol succinate, was 10 times larger than that used in the only previous double-blind study.

Patients Paired Off

Patients were paired off as closely as possible by sex and age and were then assigned a code number from a computer-generated list of paired random numbers that had been used to number the vitamin and placebo containers.

The patients kept daily track of the number of nitroglycerin tablets taken each day during the trial. They also recorded whether anginal pain was worse, better, or the same as usual and whether physical activity was less, more, or the same.

Final assessments made by the attending physicians indicated that the majority of the patients in each group—13 on vitamin E and 12 on placebo—experienced no change in their angina. One patient on the vitamin regimen was assessed as "much improved" and four others as "improved." Among the placebo takers, none were "much improved" but three were "improved" and two were "slightly improved." One was "slightly worse."

Other reactions recorded by the two groups also turned out to be quite similar. Most of the patients in each group showed little change in nitroglycerin consumption during the trial, and the majority in each group showed little change in activity score between the first and last weeks.

The net pain score for the placebo group was lower than that for the vitamin group in seven of the nine weeks, but if the last and the first weeks are compared, the over-all mean score dropped somewhat for the vitamin group and rose slightly for the placebo group.

In the second part of the trial, the investigators tested discontinuance of vitamin E therapy in seven of 15 patients who had been taking the vitamin for periods of months or years. (The same double-blind protocol was followed.)

This phase of the study yielded results that were more favorable to vitamin E therapy, the report stated. Four of the seven placebo patients experienced a worsening of original symptoms, compared with none of the eight who continued to receive regular doses.

The investigators noted, however, that this difference "was not statistically significant" and that the numbers of patients in the special trial were very small.

Also, such patients "may not have been as 'blind'" as those in the main trial, the report pointed out, since "it is conceivable" that patients accustomed to a large daily intake of vitamin E may experience the disappearance of some minor side effect, such as increased intestinal activity, and thus could be subconsciously alerted to the switch to placebo.

Discussing the failure of their double-blind trials to confirm the "dramatic effects" of vitamin E therapy claimed by other research teams, the Canadian investigators suggested two possible explanations—vitamin E is really of no value, and previous successes can be attributed to a combination of spontaneous remission and placebo effect, or else the vitamin "has a small effect, and spontaneous remissions and placebo effects make up the balance."

Clinical Trials

by Oldden

Sodium Acetate May Slow Alcohol Absorption

Medical Tribune Report

CHICAGO—Sodium acetate slows down alcohol absorption in rats and may point the way to a new pharmacologic approach to both alcoholism and gluttony in man, an Arizona team reported here.

The studies showed that when large amounts of sodium acetate were fed with alcohol to rats, the acetate delayed the emptying of the stomach and thus hindered the absorption of alcohol from the intestinal tract.

Detailing the findings to the American Chemical Society, Dr. Cleamond D. Eskelson, of the Veterans Administration Hospital in Tucson, Ariz., said that the studies were undertaken in an effort to find a method that would help "decrease inebriation time in humans" and, ultimately, "reduce the cost of sobering up the inebriated individual."

In the animal experiments, Dr. Eskelson reported, when he and his colleagues administered acetate, an alcohol metabolite, in an amount half that of the oral alcohol load, "a distinct decreased blood alcohol level was obtained, as compared to plasma alcohol levels in a control group of rats not given acetate."

Inhibited Emptying of Stomach

"Further experimentation revealed that acetate inhibited the emptying of the stomach and did not alter alcohol's oxidation," Dr. Eskelson commented. "From these studies it was concluded that there is a feedback control of alcohol's release from the stomach. The mechanism for this is:

"As alcohol is released from the stomach it is readily absorbed from the gut; this alcohol is then metabolized in the liver, producing acetate, which circulates back to the stomach, inhibiting gastric emptying. Thus, alcohol absorption is controlled by its own metabolism."

Dr. Eskelson acknowledged that there is an "obvious handicap" in requiring large amounts of acetate to produce the desired prolonged effect. But he stressed his view that the team's findings are "highly significant" in that:

"1. A method has been discovered which inhibits alcohol's absorption from the gastrointestinal tract by inhibiting the emptying of the stomach.

"2. It is probable that this method will inhibit the emptying of the stomach when alcohol is not present.

"3. The GI tract probably contains receptor sites for acetate which, when occupied by acetate, inhibit gastric emptying."

He added: "The above concepts suggest for future research that a drug (derivative of acetate) may be found which is not metabolized but could have significance not only on alcohol metabolism but in controlling food intake. This latter is important for overweight individuals and in individuals having cardiovascular disease."

Coauthors were Drs. Laurence Meeks, Larry Myers, and Robert MacDonald.

Heart Attacks Up in Japan

Medical Tribune World Service

TOKYO—Ten years ago the majority of cerebrovascular accidents in Japan occurred among hypertensive patients, but in the past decade this level has dropped 30-40 per cent, while the incidence of heart attack has climbed appreciably, mainly in the stress-ridden urban areas.

Noise Turns Hospitals Into 'Symphony Halls'

Medical Tribune Report

CHICAGO—"Noise pollution," a central service nurse told the American Health Congress, has turned hospitals into "medical symphony halls."

Wilma Leppart, R.N., of Veterans Westside Hospital, Chicago, said that most hospitals are built in a way that helps the transmission of sound.

The person in charge of central service is responsible for controlling noise, she said, and central service should be located on the ground floor along with operating, emergency, and recovery rooms. Administrative offices should be on another floor, she added.

TRIBUNE SPORTS REPORT

Low Glucose Intake Advised During Prolonged Exercise

Medical Tribune Report

SEATTLE—During prolonged exercise the concentration of glucose in ingested solutions should be minimized to achieve an optimal rate of gastrointestinal absorption, according to a study by David L. Costill, Ph.D., of Ball State University, Muncie, Ind., and three Stockholm investigators, B. Saltin, M. Soderberg, and L. Jansson.

They observed that, despite attempts to ingest sugar solutions during prolonged severe exercise, most athletes are unable to keep pace with the large fluid losses incurred through sweating. The rate of gastric emptying governs the volume of fluid that can be ingested and delivered for intestinal absorption, they noted.

Their study, presented here at the 20th annual meeting of the American College of Sports Medicine, showed that sodium chloride in ingested solutions had little effect on the rate at which the stomach emptied, but that the addition of even small amounts of glucose (2.5 Gm./100 ml.) induced a marked reduction in the rate of emptying. It was also observed that the volume of fluid remaining in the stomach 15 minutes after ingestion was significantly greater when the solution was 35° C. than when it was 5° C.

Children's Temperature Regulation Same as Adults' in Distance Runs

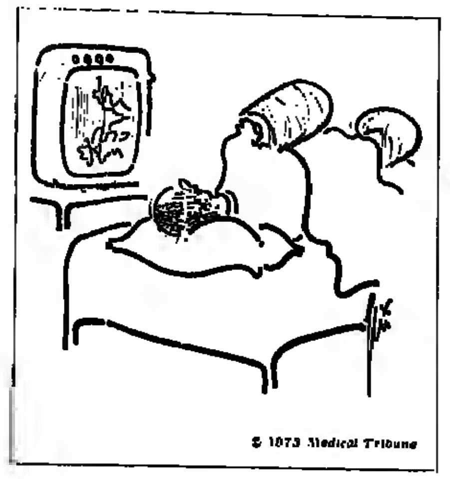
From Livermore and San Jose, Calif.

►During distance running, children have the same temperature-regulating ability as adults despite a lower sweat rate, according to a team of California investigators.

"This may be due to a greater surface area–weight ratio, which allows more heat loss by conduction and convection, although a lower work load cannot be excluded," said Dr. C. H. Brown and T. Fahey, of the Veterans Administration Hospital, Livermore, and California State University, San Jose.

After three runs of five to 13 miles, rectal temperature was 38.7° C. in five girls, compared with 39.1° in 14 women, and 38.5° in six boys, compared with 39.2° in four men. Sweat rates were considerably lower in the children: 6.4 Gm./sq. M./minute in 19 girls, against 8.5 in 29 women, and 7.0 Gm./sq.M./minute in seven boys, against 11.3 in four men. The sweat rates of the boys and girls were the same, but men had significantly higher sweat rates than women.

There was no clinical or laboratory evidence of a greater tendency for dehydration in the children than in the adults, it was reported.



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IMMATERIA MEDICA

By DUDLEY STRAUS

The Machines

• "Computers can conceal white collar crime of a magnitude undreamed of by the most optimistic of bank robbers," says *New Scientist.*

It reports, among other computer crimes, the following:

1. A New York bank teller fed false information into the bank computer, and it tucked away $1,500,000 for him.

2. A Los Angeles electronics engineer used his own phone to tap into the telephone company's computerized supply system and cabbaged over a million dollars' worth of equipment. (Don't think that we understand this.)

3. A California accountant got a computer to steal $1,000,000 for him over a five-year period.

4. A New Jersey bank employee got his bank's computer to draw $100,000 from various accounts and deposit it in the accounts of two of his coconspirators.

5. The designer of a computerized deposit system at a Midwest bank programmed it to ignore his own overdrafts; then he began passing bad checks.

All of these crimes, according to our source, were discovered by accident.

• *Science* came out, the following day, with the news that the Ervin Committee was using a Library of Congress computer to process the voluminous data it and other bodies are collecting on the subject of Watergate.

• IMBLMS (Integrated Medical and Behavioral Laboratory Measurement System), "intended to appraise the technical requirements for remote health care in space," is a joint project of HEW and NASA. It will make maximum use of computers and other machines, HEW says, and will be tested out on the Papago Indian Reservation.

Lo, the poor Indian!

• DoctorsAid is the name of an automated interviewing device for use in any hospital, clinic, "or office seeing five or more new patients a day," a press release informs us.

It can ask a selection from a total of 1,600 questions and ends up with a computer printout of "medically significant answers."

DoctorsAid? DoctorSaid?

• CLAUDE (Computer List of Anticipated and Unintended Drug Effects), we see in the *New England Journal of Medicine*, is a 9,000-entry file of effects of drugs in laboratory tests.

• The Louis B. Mayer Teaching Center at the University of Southern California School of Medicine has machines that "facilitate instructional communication," the university's news bureau tells us.

"An electronic computer response system allows students to participate individually through a push-button device on the arm of 265 seats in the 500-seat auditorium," according to a release; and we haven't the vaguest idea what goes on the other 235 seats.

The instructor—yeah, there's still an instructor—has a console that gives him a continuing visual report on class answers while an electric scanner collects the answers and feeds them to a computer, which produces an immediate printout covering the whole scene. Presumably, the products of this education will get a briefing somewhere on how to recognize a human being in case one ever turns up.

So who was that computer I seen you with last night?

Readers are invited to contribute items of 100 words or less to this column. Contributions should be mailed to MEDICAL TRIBUNE, *880 Third Avenue, New York, N.Y., 10022.*